

# *The New Jersey* **JOURNAL of Pharmacy**

New Jersey Pharmacists Association

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# Change is a Choice, Growth is a Commitment

## A Message from Incoming President, Moriah Weissman

### About me.

Greetings! As the incoming President of NJPhA, I am honored to introduce myself, review my plan for the year and announce our 144th Annual Meeting & Convention in this publication of The New Jersey Journal of Pharmacy.

I have served the executive line for the last two years as 2nd Vice President and 1st Vice President. Prior to joining the line, I supported Region 2 as their Treasurer for several years. I worked closely with the President at the time, Emil Veltre, to organize and execute our 1st Annual BBQ and Minor League Baseball Game in Montclair as well as a Networking Happy Hour in Hoboken. As a member of the executive line, I have participated in a variety of work streams including the implementation of a formal New Member Welcome Packet and processes for its distribution as well as the Student Chapter Charter and Membership process. I have assisted in updating the Association's use of technology by introducing the use of webinar capabilities and the implementation of our new website.

I earned my Doctor of Pharmacy degree from the University of Sciences in Philadelphia and I am a Certified Consultant Pharmacist (CCP). My professional experience spans from pharmaceutical industry to long term care and community clinical practice. Additionally, I work as a Medical Information Manager for Novartis Pharmaceuticals Corporation and here, serve as an APPE preceptor for PharmD students.

### *My vision for the upcoming year.*

So, what does the upcoming year look like for us? Our main purpose will be to continue to advocate on behalf of all the Pharmacists and Pharmacy Technicians in the State of New Jersey. Monitoring new legislation or regulation that can affect our profession is always a priority, and a primary member service. Our efforts on the national front focus on informing our federal representative about the positive effects the achievement of provider status (allowing pharmacists to bill and receive payment for services rendered) for pharmacists will have on the patients of New Jersey.

Our Advocacy Team actively works with APhA – American Pharmacists Association, NASPA – National Alliance of State Pharmacy Associations, NCPA – National Community Pharmacists Association, NABP – National Association of Boards of Pharmacy, various coalitions and others to protect our best interests and promote grassroots advocacy on key issues. It is not enough to influence legislation alone; we must also be vigilant about regulatory proposals. In order to impact change – our team works with the NJ Board of Pharmacy, Board of Medical Examiners, Drug Utilization Review Board and the Health Information Technology Committee to ensure pharmacists can practice to the highest level of their training and expertise.

In addition to working hard on Advocacy, I will ask our Leadership to continue to take an active role in strengthening our Association through a variety of events and opportunities for our members. I welcome your participation, and if you are interested in learning more or becoming a more active member, please find me at the Convention and I'd be glad to chat over coffee or even in the hall on the way to a session!

### *144th Annual Meeting & Convention.*

Our convention graphic aptly depicts the theme of our 144th Annual Meeting and Convention. When that light bulb in your head goes off—it stimulates ideas and new opportunities—in other words, CHANGE. Change, by itself, is a reality we face every day. It is something to embrace, and those that do embrace it, GROW. However, change and growth require one to choose a new path and work toward the opportunities it presents.

The convention, held over a period of 3 days from Friday, September 19th to Sunday, September 21st offers both continuing education programs and professional development seminars with plenty of thought-provoking information to fuel your good ideas! Concurrently, we will be running a number of Certificate Programs, including a newly developed course - *Compounding Essentials*. In light of the recent buzz around compounding, this certificate course was developed to introduce or supplement pharmacist and pharmacy technician sterile and on-sterile compounding education in a variety of settings.

**Friday** will be filled with networking events and business meetings; the evening will kick off the official start to the Convention with our Welcome Reception and after-hours social events.

**Saturday** will be a full day including continuing education programs, professional development seminars, student programming, the Annual Meeting, networking events, a full exhibition hall, our 2nd Annual Poster Session, an evening reception and after-hours social events.

**Sunday** will mark the end of our 144th Annual Meeting & Convention; it will include additional continuing education programs, the full exhibit hall, networking events and our Keynote Speaker who will be reviewing the National Action Plan for Adverse Drug Event (ADE) Prevention.

**Take advantage of Early Bird Registration Discounts if you register before August 1, 2014!**

**Looking forward to seeing you there!**

Moriah Weissman, PharmD, CCP  
2013-2014 1st Vice President  
2014 Convention chair

## The New Jersey Pharmacists Association

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Click on the home page banner for  
Annual Meeting and Convention for all the details.



**144<sup>th</sup> Annual Meeting & Convention**  
The Berkeley Oceanfront Hotel  
Asbury Park, New Jersey  
**September 19-21, 2014**

### Mission Statement:

*To advance the profession of pharmacy, enabling our members to provide optimal care to those they serve.*

## **President's Letter**

Dear NJPhA Members:

If you heard me speak at convention, you have heard me suggest that one way to get involved is to nominate someone for an award. In this issue we present the myriad of awards conferred by NJPhA (or through NJPhA by other organizations) each year.

We know there are many pharmacists out there leading the charge for patients and the profession - but we don't know them by name or specifically how they are doing this. Here's where you come in: You Do!!

Just like any other membership organization, we rise and fall with the contributions and participation of our Membership.

Take a moment to read the list of awards and then think through all the pharmacists (there are some non-pharmacist awards, too) you know and submit at least one nomination. We promise it won't take much time. Being recognized by your peers is one of the most gratifying experiences a professional can have. Being chosen from tens (maybe hundreds!) of applications would only make it more special. Won't you take a moment to do that for someone you respect?

Best,  
Carrie

Carrie Corboy, RPh, PharmD, CCP  
<http://www.linkedin.com/in/carrieccorboy>  
President, New Jersey Pharmacists Association (NJPhA)

## **From The Editors' Desks...**

Dear Colleagues,

On the heels of Public Health week, where our issue focused on the pharmacist's role in public health issues, this issue focuses on neurology and psychiatry. New medications vortioxetine, lorcasertin, and eslicarbazepine are introduced in this issue, in addition to a free continuing education activity on treatment of post partum depression. We are grateful to the Ohio Pharmacists Foundation, Inc., for once again sharing a continuing education activity with our members. The application of pharmacogenetics is growing and its role in medication selection and dosing is still being evaluated.

As our Journal evolves, we continue to recruit authors and peer reviewers. Our upcoming issues focus on infectious diseases and endocrinology. Please contact us if you have an idea for an article, or would like to participate in the Journal.

We wish you a happy summer!

Regards,  
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## ***Message from the CEO***

### **Be Ready for What is Ahead**

Every day is different. There are ‘good’ days, and ‘bad’ days. Though measured in various ways, I suspect the *good days* are those when you accomplish your goals, put your plan in action, or complete a difficult task. *Bad days* are, well, those days when nothing goes your way—the essence of the inability to CHANGE!

Frequently, change is a response to an environmental condition—one where the change has occurred before you could prepare for it. The uncertainty, and fear or reluctance to embrace this new condition causes angst and trepidation. Day turns into night; winter turns into spring (OK, maybe not this year!). All of it is a form of change, and each individual has the choice to commit to it or ignore it.

Today, everything is electronic. We can create accounts, manage our preferences, and navigate the internet without restriction, but many prefer that life offer them more ‘customer service’ the way it used to be....

Is all this change bad? There was a time when light bulbs were new, cars were new, dishwashers were new, and all represented significant change to the daily routine of life. Do you want to give up these advancements and new-fangled items?

NJPhA’s 144<sup>th</sup> Annual Meeting and Convention is about CHANGE. The continuing education programs and professional development seminars planned will guide attendees through changes within the profession, present opportunities to acquire new skills or enhance your level of expertise in a specific disease state. Confirm your commitment to the profession of pharmacy by joining us in Asbury Park from September 19 through September 21.

Change illustrates your successes based on your commitment to your goals. If you want to be a pharmacist, pharmacy technician or student at the top of your game, providing patients with the highest level of care, learning about new treatment protocols, new medication safety requirements, disease management and treatment options, then you plan to change! See that was not so bad!

There is change all around us—just look.

Elise M. Barry

### **PHARMACY ATTORNEYS HELPING PHARMACISTS**

In a time in which the profession of pharmacy is under heightened scrutiny, it is *essential* to make sure your rights are being protected.

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## Call for 2014 Award Nominations

Who inspires you? A neighborhood pharmacist who donated medication to a family working through hard times?

A pharmacy school instructor who helped you master that topic you initially thought was impossible to comprehend?

NJPhA provides members with an excellent way to thank fellow NJPhA members—colleagues, friends, mentors—or any other pharmacy professional who made a difference in your career. Each year at the Annual Meeting and Convention, NJPhA recognizes member-nominated award recipients for their contributions and achievements.

The following list outlines all the categories in which nominations can be submitted. The application form is available on the website under the Membership tab. Select Awards and scroll to the application form and click submit!

Few things are more gratifying than peer-recognition. Who will you nominate today?

Award Name	Award Description
<b>Rosario J. Mannino Award</b>	This award honors President-Emeritus Rosario J. Mannino, and is given for meritorious service to the profession of pharmacy and the New Jersey Pharmacists Association.
<b>Bowl of Hygeia</b> Sponsored by APhA Foundation and NASPA	Sponsored by National Alliance of State Pharmacy Associations (NASPA) to a living, NJ licensed pharmacist who has compiled an outstanding record of community service that, apart from the practice of pharmacy, reflects well on the profession.
<b>Andrew J. Preston Political Action Award</b>	Sponsored by past President and PAC Chairman Andrew J. Preston, this award is presented to the NJPhA member exhibiting outstanding effort in the political arena to benefit the profession and our patients.
<b>Donald J. Wernick Academic Achievement Award</b>	Presented to an academician who has performed outstanding service for our profession and NJPhA.
<b>Frederick B. Kilmer Award</b>	Dr. Kilmer, a former NJPhA president, established the concept of research at J&J that became a standard for much of the pharmaceutical industry. He was a prodigious writer who valued articulate writing as a means of improving the pharmacy profession and the health of our citizenry.
	Though Dr. Kilmer's bequest to recognize excellence in pharmacy was depleted many years ago, the award has been given since 1938. All members, with the exception of educators and laboratory workers, are eligible.
<b>NASPA Excellence in Innovation Award</b> Sponsored by Upsher-Smith	Sponsored by NASPA, a nominee should be a practicing pharmacist within New Jersey who has demonstrated innovative pharmacy practice resulting in improved patient care.
<b>Jesse Gaynor Award</b>	Presented to a consultant pharmacist who has shown meritorious service and dedication to the practice of pharmacy.
<b>Mortar &amp; Pestle Award</b>	Authorized by the Board of Trustees, the Mortar & Pestle Award is given to an individual who is not a pharmacist, but who by virtue of his or her activity, has contributed to the profession of pharmacy and the public-at-large.
<b>William H. McNeill Award</b>	This award recognizes outstanding community service work by an NJPhA member for work done in the preceding year or years.

Award Name	Award Description
<b>Pharmacist Mutual Distinguished Young Pharmacist Award</b>	<p>Presented to an outstanding pharmacist who has worked for the profession of pharmacy and who graduated in the past ten years. This award is presented to a pharmacist who best meets the following guidelines:</p>
	<ul style="list-style-type: none"> <li>• Licensed to practice in New Jersey</li> <li>• Current membership in NJPhA</li> <li>• Practices retail, institutional, managed care, or consulting pharmacy in the year selected</li> <li>• Participation in national pharmacy associations, professional programs, state association activities, and/or community service</li> </ul>
<b>Pharmaceutical Industry Award</b>	<p>Presented to a representative of the pharmaceutical industry who has advanced the profession through educational efforts or support to the profession.</p>
<b>Independent Pharmacist of the Year Award</b>	<p>Supported by Buy-Sellapharmacy.com, this award is presented to a practicing pharmacist who has demonstrated exemplary service to his/her patients and the community.</p>
<b>Cardinal Health Generation Rx Champions Award</b>	<p>Presented to a pharmacist in recognition of efforts to prevent prescription drug abuse and outstanding service to the pharmacy community to raise awareness of this serious public health problem.</p>
<b>Sidney B. Gilman Pharmacy Technician Award</b>	<p>Presented to an NJPhA Pharmacy Technician member in recognition of Individual excellence and outstanding service to the pharmacy profession.</p>

**Awards nominations are open, and the nominations can be completed online at <http://njpharmacists.org/membership/awards> or go to <http://njpharmacists.org>, click on the Membership tab at the top of the home page, and select Awards from the dropdown menu.**

## Your Nominee will be in Good Company!



Ron Mannino with Dr. Sandra Moore, recipient of the 2013 Rosario J. Mannino Award given for meritorious service to the profession of pharmacy and the New Jersey Pharmacists Association.



*The Lifetime Service Award is presented to an individual whose experience and contribution to the Association and our profession has had a profound and lasting effect. The recipient is universally respected and admired by their peers and has reached a professional stature attained by few.*

*In 2013, NJPhA honored Dr. Steven Zlotnick for his outstanding accomplishments. Steve's service to NJPhA covers many years and many positions.*



Dr. Carrie Corboy - Pharmaceutical Industry Award, Eileen Fishman, RPh. - Bowl of Hygeia Award, Dr. Grace Earl - Donald J. Wernik Academic Achievement Award, Dr. Anne Crochunis - NASPA Excellence in Innovation Award, Dr. Moriah Weissman - Pharmacists Mutual Distinguished Young Pharmacist Award

# Clinical Overview of Lorcaserin

By Joseph Schafer, PharmD Candidate and Stacy Elder, PharmD, BCPS  
Philadelphia College of Pharmacy, University of the Sciences

Obesity is a growing epidemic in the United States and affects over 100 million Americans, meaning that one in every three people is affected by the disease. In order to be diagnosed, an individual needs to have a body mass index (BMI) of over 30.<sup>1</sup> It is not just a simple definition of having excess body weight, however. It is a disease that is associated with many comorbidities including hypertension, dyslipidemia, and type 2 diabetes. All of these conditions pose an additional risk of complications including fatal events such as heart attack and stroke. In 2008, a recorded \$147 billion was spent to treat complications stemming from obesity.<sup>2</sup>

The prevalence of obesity has been steadily rising each year since the 1990's.<sup>1</sup> As obesity has increased, so has the search for new methods of weight loss. Some patients cannot achieve optimal weight loss with diet and exercise alone, so alternative methods have been sought to help solve this problem.<sup>3</sup> Medications have a growing role in the weight loss market, with several drugs (orlistat, phentermine-topiramate) indicated for obesity approved within the last decade.<sup>4</sup> The most recent prescription weight loss medication approved by the United States Food and Drug Administration (FDA) is lorcaserin (Belviq®).

Lorcaserin is a selective serotonin “5-HT” agonist that acts on anorexigenic neurons in the hypothalamus to reduce hunger and promote hypophagia.<sup>5</sup> The 5-HT receptors have receptor subtypes known as 2B and 2C. While the 2B and 2C receptors are located mostly in the hypothalamus, the 2B subtype are also located in the heart valves. Stimulation of these 2B receptors may lead to cardiac complications such as valvopathy. Unlike prior medications with similar mechanisms of action, lorcaserin is selective for 2C receptors, showing 100 times more affinity than for 2B receptors. This receptor selectivity theoretically eliminates the possible cardiac adverse events.<sup>5</sup>

The FDA indications for lorcaserin include a BMI over 30, or a BMI over 27 with at least one comorbid condition (hypertension, type 2 diabetes, dyslipidemia, etc).<sup>5</sup> In the studies showing greatest clinical benefit, lorcaserin was utilized in conjunction with lifestyle modifications. The medication is administered as a 10 mg dose by mouth twice daily (BID), and discontinuation is appropriate if 5% weight loss does not occur by week 12. Lorcaserin can be taken with or without food with plasma levels reaching a peak at around 2 hours. It has high bioavailability and is rapidly absorbed. The plasma half-life is approximately 11 hours, and the drug is extensively metabolized by the liver.<sup>5</sup>

The first phase III study done to evaluate lorcaserin is the Behavioral Modification and Lorcaserin for Overweight and Obesity Management (BLOOM) randomized clinical trial.<sup>6</sup> The study enrolled 3182 obese and overweight patients to take lorcaserin 10 mg daily, lorcaserin 10 mg BID, or placebo for 104 weeks. At baseline, most patients included were middle-aged Caucasian females. The primary endpoints of BLOOM were change in body weight, proportion of subjects that reached 5% body weight reduction, and then the proportion that reached 10%

body weight reduction. At the end of the first 52 weeks, patients were randomized a second time to placebo or lorcaserin to determine the sustainability of weight loss. The additional endpoint studied was the proportion of patients who maintained the original 5% weight reduction at the end of year two. Secondary endpoints included changes in lipid values, glycemic variables, physical characteristics, and blood pressure at 52 weeks.<sup>6</sup>

Results for the BLOOM trial showed that 47.5% of patients receiving lorcaserin BID lost 5% or more of their baseline body weight, as compared with 20.3% of patients receiving placebo ( $p<0.001$ ) at the end of year one.<sup>6</sup> Lorcaserin patients lost an average of 5.8 kg in the first year, as compared to 1.6 kg in the placebo group. For secondary endpoints, all patients who received lorcaserin had improved lipid values (total-c, LDL-c, TG), glycemic variables (fasting glucose, fasting insulin), and blood pressure (systolic and diastolic). During year two of the study, 67.9% of patients continuing to take lorcaserin maintained the 5% weight loss, compared to the 50.3% of those who began taking placebo ( $p<0.001$ ). Cardiac valvopathy was no more significant in the lorcaserin groups than placebo.<sup>6</sup>

The second study largely contributing to the approval of lorcaserin is the Behavioral Modification and Lorcaserin Second Study for Obesity Management (BLOSSOM) trial.<sup>7</sup> BLOSSOM enrolled 4008 overweight and obese patients and evaluated the same primary and secondary endpoints that were utilized in BLOOM. The general demographics were similar, and the main procedural difference was that BLOSSOM was only 52 weeks in duration. Results were similar to those seen in BLOOM as 47.2% of those in the lorcaserin BID group lost at least 5% of their body weight when compared to 25% in the placebo group ( $p<0.0001$  for each). In the lorcaserin BID group, 22.6% lost 10% of their body weight, as opposed to 9.7% of those in the placebo group. Patients receiving lorcaserin BID lost an average of 5.8 kg, whereas patients receiving placebo only lost 2.9 kg ( $p<0.001$ ). Secondary endpoint results were similar to BLOOM.<sup>7</sup>

A third clinical trial focused solely on lorcaserin's efficacy in overweight/obese diabetic patients: Behavioral Modification and Lorcaserin for Obesity and Overweight Management in Diabetes Mellitus (BLOOM-DM) Study.<sup>8</sup> The primary and secondary endpoints were the same as BLOOM and BLOSSOM, but this study only included patients with type 2 diabetes and elaborated on the glycemic secondary endpoints. The study enrolled 604 patients over 52 weeks. The results of each endpoint were similar to the BLOOM and BLOSSOM trials. Each glycemic endpoint (HbA1c, HOMA-IR, fasting glucose) showed statistically significant favorability associated with the lorcaserin group in diabetic patients.<sup>8</sup>

While there was no increase in valvulopathy in clinical trials, lorcaserin has several safety issues that healthcare providers need to consider. Lorcaserin is contraindicated in pregnancy as it is pregnancy category X, and all women of childbearing potential should be evaluated before initiating this, or any other weight loss drug.

Breastfeeding should be avoided since it is not known if lorcaserin is passed into breastmilk. The most common side effects observed during treatment include upper respiratory infections (12.7%), headache (15.6%), dizziness (8.7%), nasopharyngitis (12.5%), and nausea (9.1%).<sup>6,7</sup> The risk for serotonin syndrome has not been established, but caution should be exercised when considering combination with serotonergic agents. It is reasonable to monitor for valvulopathy as the drug's use increases in the general population, despite its lack of affinity for cardiac receptors and lack of increased valvulopathy in clinical trials.

In patients taking antidiabetic medications, weight loss attributed to lorcaserin could lead to hypoglycemia. Therefore, blood glucose needs to be monitored in diabetic patients. It should also be noted that lorcaserin was not studied in patients on insulin therapy. The BLOOM-DM study only included those using either metformin or sulfonylureas. The most common adverse reactions in diabetic patients included hypoglycemia (7.4%), headache (14.5%), back pain (11.7%), cough (8.2%), and fatigue (7.4%).<sup>5,8</sup>

Lorcaserin is proven effective for at least 5% weight reduction over the course of one year in overweight or obese patients (BMI >30 or BMI >27 with at least one comorbid condition) with or without diabetes, between the ages of 18-65 years, as well as maintaining weight loss once initial goals are reached. All results were seen in large-scale studies in combination with diet and exercise. Future research on the effect of lorcaserin on patient outcomes such as mortality and progression to chronic disease states will be important to establish any clinical significance of the weight loss associated with the medication.

## About the Authors

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# Aptiom®: New Drug Approved for Partial Seizures

by Ellen McKnight, PharmD Candidate; LaKeisha Williams, PharmD, MSPH

Approximately 65 million people are living with epilepsy and 150,000 new cases of epilepsy are discovered each year.<sup>1</sup> Epilepsy, also known as a seizure disorder, is a neurological condition that affects the nervous system.<sup>1</sup> A seizure results from a sudden electrical surge in the brain caused by an imbalance of electrical activity, which causes brain cells to excite or inhibit message delivery in neighboring neurons. This neurological disorder is thought to be related to brain injury caused by a traumatic event or genetic predisposing factors, but in many cases, the cause is unknown. A person is usually diagnosed with epilepsy after they have experienced two or more epileptic seizures from a cause unrelated to a known medical condition. The two major groups of seizures are primary generalized seizures and partial seizures. Primary generalized seizures are initiated by widespread electrical discharges that involve both hemispheres of the brain simultaneously. Partial seizures are initiated by an electrical discharge at a limited area in the brain.<sup>4</sup> Treatment options for epilepsy include antiepileptic drugs (AEDs), vagus nerve stimulation, and surgery, such as focal resection and hemispherectomy (removal of areas of the brain in which seizures frequently occur). Studies have also shown that even diets, such as the ketogenic diet, consisting of high fats and low carbohydrates, can reduce the occurrence of seizures.<sup>4</sup>

Neuronal excitability is crucially determined by sodium mediated currents.<sup>2</sup> A minor increase of sodium current has been shown to drastically alter chemical components in the brain and facilitate hyperexcitability, or the rapid firing of electrical impulses in neurons, which causes seizures. The persistent sodium current, or  $I_{NaP}$ , has been proven to amplify a neuron's responses, therefore enhancing its repetitive firing capacity.<sup>2</sup> For this reason, the role of the persistent sodium current in seizure behavior constitutes an interesting focus in epilepsy research.<sup>2</sup> Studies have shown that an increase in  $I_{NaP}$  is associated with epilepsy syndromes with sodium channel mutations. These channel mutations can affect different proteins that form the sodium channel complex.<sup>2</sup>

Aptiom®, the marketed name for eslicarbazepine acetate, is a voltage sodium gate inhibitor that was approved by the U.S. Food and Drug Administration (FDA) on November 8, 2013, as an adjunctive treatment of partial onset seizures. Prior to its release in the U.S., eslicarbazepine acetate had been licensed for clinical use in Europe in 2009 as Zebinix®, Exalief®, and Stedesa®. Eslicarbazepine acetate reduces the frequency and/or severity of seizures by inhibiting the voltage gated sodium channel, which regulates sodium ion concentrations inside and outside of neurons.<sup>3</sup> It is available as an oral tablet in the strengths of 200 mg, 400 mg, 600 mg, 800 mg, and can be taken once daily crushed or whole with or without food. Eslicarbazepine acetate has high absorption in the gastrointestinal tract following oral administration. Bioavailability is also high because the amount of metabolites recovered in the urine corresponds to more than 90% of an eslicarbazepine dose.<sup>6</sup> Studies have shown that a once-daily dose of 800 mg appears to offer the optimal maintenance add on treatment regimen in most people who experience epileptic seizures. Some patients may benefit from the maximum recommended maintenance dosage of 1,200 mg once daily, although this

dosage is associated with an increase in adverse reactions.<sup>3</sup> Patients with impaired renal function whose creatinine clearance is less than 50 mL/minute require an initial dose of 200 mg orally once daily for 2 weeks followed by a maintenance dose of 400 mg orally once daily. Patients with severe hepatic impairment should avoid anti-epileptic therapy with this medication.<sup>5,7</sup> Special considerations must be given to elderly population as only very few clinical trials have been conducted in patients aged 65 and over. However, of the small amount of patients aged 65 and older, approximately 80% of elderly patients with epilepsy had good response to therapy with AEDs and remained seizure free for at least a year, according to Verotti et al.<sup>6</sup> Serum sodium and chloride levels should be monitored during maintenance treatment of eslicarbazepine acetate, especially in patients at risk for hyponatremia. Monitoring should also occur if symptoms of hyponatremia develop. Patients taking eslicarbazepine acetate should also be closely monitored for changes in mental behavior that may indicate suicidal thoughts and depression. Contraindications are hypersensitivity to eslicarbazepine, oxcarbazepine, and other parts of the formulation.<sup>5</sup> Adverse effects were usually mild to moderate in intensity, and the most common were dizziness, somnolence, nausea, diplopia, headache, vomiting, abnormal coordination, blurred vision, vertigo, and fatigue.<sup>5</sup>

In three phase 3 randomized, double-blind, placebo-controlled, multi-center safety and efficacy trials, a statistically significant reduction in seizure frequency was observed with eslicarbazepine acetate treatment at doses of 800 mg/day in studies 1 and 2 ( $p=0.047$ ;  $p=0.006$  vs. placebo). Significant reduction were also seen at doses of 1,200 mg/day in all 3 studies, respectively ( $p=0.001$ ;  $p=0.042$ ;  $p=0.004$  vs. placebo). Approximately 41% and 32% of adults randomized to eslicarbazepine acetate experienced a 50% or greater reduction in seizure frequency (responder), compared to 22% of those randomized to placebo (1,200 mg/day and 800 mg/day, respectively).<sup>8</sup>

Eslicarbazepine acetate is not recommended for patients less than 18 years of age.<sup>3</sup> It appears to be a safe and effective drug with very low potential for drug-drug interactions. However, several trials are currently being conducted to further assess the efficacy of eslicarbazepine acetate.

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***It is with great sadness that we report the passing of two individuals with deep roots in NJPhA.***

### ***Alvin Geser***

Alvin was born and raised in Baltimore MD. He graduated from the University of MD School of Pharmacy in 1950 and The University of MD School of Law in 1957. In 1961, Geser moved to NJ to assume the position of Executive Officer of NJPhA. During his professional career, Mr. Geser was involved in initiating healthcare legislation. Of special importance to him was the development of a proposal in 1965 by the pharmacy practice committee to reduce the number of children's aspirin tablets per bottle to 36 in hopes of reducing the more than 300 annual children's aspirin deaths.

Mr. Geser was a frequent speaker at Rutgers College of Pharmacy and served on the Dean's committee at Rutgers and PCP. An author of several published articles, Mr. Geser was a recipient of the President's Award of the American Society of Pharmacy and Law and served as honorary president of APhA in 1995.

### ***Frank Pinchak***

We are saddened by the passing of Frank Pinchak, South Paterson pharmacist and former president of NJPhA on April 5. A graduate of Rutgers School of Pharmacy in 1943, he operated the pharmacy founded in 1919 by his father Morris. During his time as president of the Passaic County Pharmacists Association, Pinchak introduced an education program in response to two cases of child poisonings. His aim was to call the public's attention to the tragedies caused by medications and household products improperly stored within reach of young children. The centerpiece of the project was a poster, "Save your Child-Keep Medicines out of Reach-Safe Storing Saves Lives."

As president of NJPhA, Pinchak helped establish Poison Control Centers in New Jersey hospitals. This ultimately led to the formation of the Poison Control Center at the University of Medicine and Dentistry in Newark. The center, which was the first in the nation, responded to over 400 poisonings a day. In 1996, Pinchak was a curator of a pharmacy exhibit at the Paterson Museum. The exhibit contains over 700 patent medications of the 1920s from the Pinchak Pharmacy.

### **Upcoming CE Schedule**

Date	Location	Title	Contact hours
July 13	New Brunswick, NJ	Pharmacy Based Immunization Delivery Certificate – Live component (prior home study required)	8.0
July 13	New Brunswick, NJ	Pharmacists & Patient-Centered Diabetes Care Certificate-Live component (prior home study required)	8.0
August 7	Secaucus, NJ	Preventing Prescription Drug Abuse	1.5
August 9	Hamilton, NJ	Addiction-Choice vs. Chronic Disease	2.0
August 13	Egg Harbor, NJ	Lyme's Disease and Drug-induced Photosensitivity	1.5
September 3	Washington Township, NJ	Prescription & Over-the-Counter Drug Abuse in the Elderly Population	1.5
		Medication Therapy Recommendations for Geriatric Patients	1.5
September 17	Voorhees, NJ	Unbreak My Heart: HFrEF and HFpEF	1.5
September 19-21	Asbury Park	144th Annual Convention	Multiple
October 8	Toms River, NJ	Treatment of Attention-Deficit Hyperactivity Disorder (ADHD)	1.5
November 16	Freehold, NJ	Herbal, Vitamin, and OTC Drugs	1.5

For full details and to register for any of these programs, please visit <http://njpharmacists.org/events>, and click on the calendar date for each program.

# Vortioxetine: A Novel Multimodal Antidepressant

by Dongmi Kim, PharmD, BCPS, BCPP and Ligia Westrich, PhD, RPh

## Introduction

Major depressive disorder (MDD) is a common disorder characterized by symptoms that impact a person's ability to function as an individual and within the society. The hallmark symptoms of MDD are depressed mood, anxiety, diminished enjoyment of activities the individual previously enjoyed and having suicidal thoughts.<sup>1</sup> Persons may experience one or several depressive episodes within their lifetime.<sup>2</sup>

The estimated lifetime prevalence of MDD is 13-16% in the U.S. population.<sup>3</sup> Current data suggest that the pathophysiology is heterogeneous in origin and different patients may benefit from different treatment modalities. American Psychiatry Association recommends pharmacotherapy for the treatment of mild, moderate and severe depression, along with psychotherapy and ECT in select patient populations.<sup>4</sup> In clinical settings, pharmaceuticals are the most frequently utilized treatment modality for depression.<sup>5</sup> The goals of antidepressant therapy are reduction of depressive symptoms, restoration of the patient's baseline functioning and prevention of relapse and recurrent episodes.

Currently available antidepressants are classified based on their mechanism of action as: selective serotonin reuptake inhibitors (SSRI), serotonin/norepinephrine reuptake inhibitors (SNRI), tricyclic antidepressant (TCA), monoamine oxidase inhibitors (MAOI) and others. Since the effectiveness of available antidepressants is comparable between the various classes and within each class, the selection of an appropriate antidepressant depends on safety, tolerability, cost, pharmacological factors and prior response. In fact, the Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) trial has shown that patients who fail on their initial antidepressant may achieve symptom remission with a subsequent antidepressant with a different mechanism of action.<sup>6</sup>

This paper describes the clinical efficacy data, pharmacology, monitoring parameters and place in therapy of vortioxetine (Brintellix – Lundbeck; Takeda), an oral antidepressant that was approved by the FDA on September 30, 2013 for the treatment of MDD. Vortioxetine is a serotonin reuptake inhibitor, with additional pharmacological properties whose clinical benefit remains to be studied. It is available as 5, 10, 15 and 20 mg oral tablets. The recommended starting dose is 10 mg once daily. The dose may be increased to 20 mg as tolerated.<sup>7</sup>

## Pharmacology

The serotonin system in the CNS plays a key role in the pathophysiology of MDD. Based on the serotonin hypothesis for depression, pharmacologically-induced manipulations of the serotonin system in patients with MDD may improve their mood and functioning.<sup>8</sup> Vortioxetine acts on the serotonergic system, enhancing availability of serotonin (5-HT) in the synaptic cleft. However, unlike other antidepressants that work solely via inhibition of 5-HT reuptake, vortioxetine possesses multiple mechanisms of action. It inhibits 5-HT<sub>1D</sub>, 5-HT<sub>3</sub>, and 5-HT<sub>7</sub> receptor activity, and enhances the activity of 5-HT<sub>1A</sub> and 5-HT<sub>1B</sub> receptors,

in addition to inhibiting serotonin reuptake. The contribution of the individual serotonin receptor subtype activity to the antidepressant effect has not yet been established in humans.<sup>4</sup>

## Pharmacokinetics

Bioavailability of vortioxetine is 75%, with or without food. Vortioxetine is metabolized through oxidation via cytochrome P450 (CYP450) isoenzymes (CYP2D6, CYP3A4/5, CYP2C19, CY-P2C9, CYP2D6, CYP2C8 and CYP2B6) followed by glucuronidation and excretion in urine (~59%) and feces (~26%) within 48 hours. The mean half-life is about 66 hours. A maximum dose of 10 mg/day of vortioxetine is recommended for use in known poor metabolizers (due to decreased activity of CYP2D6) or with concomitant administration of strong CYP2D6 inhibitors (bupropion, fluoxetine, paroxetine, or quinidine). An increase in dose is suggested during administration of vortioxetine with strong CYP3A4 inducers (phenytoin, carbamazepine, or rifampin). There are no dose restrictions for patients with renal or hepatic impairments.<sup>4</sup>

## Clinical Trials

The efficacy of vortioxetine in the treatment of patients with MDD has been evaluated in several placebo-controlled, short-term (6-8 weeks) and one long-term (24 weeks) clinical studies.<sup>9,10,11,12,13,14,15</sup> Most short-term trials assessed change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score of vortioxetine compared to placebo as the primary outcome measure, with the exception of two trials that assessed the Hamilton Depression Rating Scale (HDRS-24). The long-term study assessed the time to relapse of MDD as the primary outcome.<sup>15</sup> Patients were required to have a current diagnosis of MDD with symptoms rating at or above a pre-specified threshold on at least one rating scale. Patients with other potentially confounding comorbidities were excluded. Vortioxetine was tested at doses of 1, 2.5, 5, 10, 15 and 20 mg/day, administered once daily without regards to mealtimes. The age of the participants generally ranged from 18 to 75 years, except for one trial that recruited elderly ( $\geq 65$  years) patients.<sup>14</sup> Vortioxetine was superior to placebo in reducing symptoms of MDD at doses of 1, 5, 10, 15 and 20 mg/day. In the long-term study, the proportion of patients in sustained remission who relapsed by week 24 (defined as MADRS  $\geq 22$ ) was significantly lower for patients who were on vortioxetine 5 or 10 mg/day compared to placebo.<sup>15</sup> In all trials, vortioxetine was generally well tolerated, with the most common adverse effects being nausea, vomiting and constipation compared to placebo.

Patients with MDD who had an inadequate response to SSRI and SNRIs were switched over to vortioxetine in a randomized study (REVIVE). As early as week 4, the patients showed a statistically significant response in MADRS.<sup>16</sup> The efficacy and tolerability of vortioxetine has also been assessed in adults with generalized anxiety disorder (GAD). In two completed randomized trials, vortioxetine did not improve symptoms of GAD.<sup>17,18</sup> One randomized placebo-controlled trial evaluated the efficacy of vortioxetine on cognitive dysfunction associated with MDD as the primary efficacy outcome measure.<sup>19</sup> Vortioxetine 10 and 20 mg/

day were significantly superior to placebo on the standard tests measuring executive functioning, processing speed, attention and memory. To assess the aforementioned parameters, the authors used objective psychological tests, such as the Digit Symbol Substitution Test (DSST).

### Warnings/Adverse drug reactions

It is recommended that vortioxetine doses over 15 mg/day be tapered down to 10 mg/day for one week prior to its discontinuation to avoid potential adverse effects (such as headache and muscle tension). A boxed warning regarding the increased risk of suicidal thoughts and behaviors in teens and young adults taking antidepressants is included in the prescribing information for vortioxetine. To avoid the risk of serotonin syndrome, therapy with vortioxetine should begin at least 14 days after discontinuation of an MAOI and if needed, an MAOI should be given at least 21 days after discontinuation of vortioxetine. Concomitant administration of vortioxetine and MAOIs, such as linezolid or IV methylene blue, is contraindicated. Vortioxetine has not yet been evaluated for use in pediatric patients. Other adverse reactions in the boxed warning include: abnormal bleeding (caution in patients taking non-steroidal anti-inflammatory drugs), activation of mania/hypomania and hyponatremia, for which monitoring is advised. Vortioxetine is classified as pregnancy category C.

### Place in Therapy

Vortioxetine is a safe and efficacious antidepressant in the treatment of MDD in adults older than 18 years. While the therapeutic effect of vortioxetine is likely to be similar to that of other antidepressants, the absence of cognitive slowing, sexual dysfunction and drug-drug interaction potential can be beneficial to select patient populations. Additional clinical studies are essential to confirm the potential effect of vortioxetine in improving cognitive dysfunction in depressed patients. As the STAR\*D trial suggests, patients who fail on previous antidepressant therapy may benefit from switching to vortioxetine for the management of MDD.

### Conclusion

Vortioxetine is a new antidepressant indicated in the treatment of MDD in adults older than 18 years. Vortioxetine is generally safe and well tolerated. Its efficacy in the treatment of MDD has been evaluated and confirmed across multiple clinical trials.

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## Practice Spotlight:

The Ernest Mario School of Pharmacy PGY-2 specialty residency in neuro-psychopharmacology is a 1-year residency that offers training in clinical services, research, and academia. The psychiatric and neurologic services are offered as a collaborative effort through Princeton House Behavioral Health, Monmouth Medical Center, Robert Wood Johnson University Hospital, and Rutgers, The State University of New Jersey, Ernest Mario School of Pharmacy. All residency directors and preceptors are faculty members of the Ernest Mario School of Pharmacy and are also clinical pharmacists at the primary residency practice sites. As a resident, I am involved in the same activities as the preceptors of each site, while completing my own independent projects and research. It is my goal as a resident to assist the preceptors with their practices, emulate their behaviors, and serve as an educator to the students of the Ernest Mario School of Pharmacy through mentorship on clerkship rotations and didactic lectures at the university.

The main practice site of Mei T. Liu, PharmD, BCPP, Assistant Clinical Professor and residency director is Princeton House Behavioral Health (PHBH). With the exception of the resident, there are no additional pharmacists onsite. PHBH is associated with University Medical Center of Princeton at Plainsboro (UMCPP) and is a stand-alone 100-bed inpatient psychiatric hospital. Services offered at the hospital include adult psychiatry, adult dual diagnosis, adult medical detoxification, adult addiction recovery, adolescent detox and addiction recovery, first responder treatment services, short-term care facility, and electroconvulsive therapy. It is also associated with 5 outpatient sites across New Jersey. In addition to attending daily rounds in order to make appropriate pharmacotherapy interventions to the inter-disciplinary treatment teams, it is the goal of the clinical pharmacist and resident to design, monitor, and evaluate treatment goals for patients that consider patient-, disease- and drug-specific information and ethical considerations. The clinical pharmacist and resident also lead medication education groups within each unit, provide individualized counseling sessions, present educational in-services to patients, pharmacy staff members and the interdisciplinary team, and supervise students on clerkship rotations.

The main practice site of Megan Maroney, PharmD, BCPP and residency preceptor is the Alexander Pavilion at Monmouth Medical Center. Alexander Pavilion is a 4-floor, 62-bed psychiatric facility which offers similar services to PHBH, including adult psychiatry, short-term care facility, and children's crisis intervention services. It is also associated with an outpatient clinic which offers an intensive outpatient program and a partial hospitalization program. The inpatient clinical pharmacy services offered at this site are similar to those offered to the team at PHBH. In the outpatient clinic, the clinical pharmacist and resident also lead medication education groups, offer consultant services, and manage samples and medication inventories.

Robert Wood Johnson University Hospital serves as the main site for the neurology component of the residency. The majority of the time spent by the resident is within the adult and pediatric

outpatient clinics, though there is opportunity for inpatient rotations as well. This is the main practice site of Mary Wagner, PharmD, MS, Associate Clinical Professor and co-director of the residency program. Each day that I am onsite in the outpatient pediatric or adult neurology clinics, I work with a different provider, each of whom has his own specialty. The physician and I work as a team throughout the day to evaluate patients, make assessments, and create plans of care in a collaborative manner. In the outpatient clinics, I serve as the main drug information resource for the providers and am often consulted to research drug information questions and to assist providers with their independent research projects.

The other practice site that is not specific to neuro-psych but at which I have spent much of my time has been the Rutgers-FOCUS Wellness Center (FOCUS) in Newark, NJ. FOCUS is a nurse-managed facility that has established an inter-professional collaborative practice model for an urban, medically underserved, and vulnerable population. The main goals of FOCUS are to provide patients with a holistic treatment approach through the expertise of advanced practice nurses, community health nurses, social workers, and pharmacists, as well as provide an interdisciplinary learning environment for the students of Rutgers College of Nursing, School of Social Work, and School of Pharmacy. Services provided through FOCUS include primary care, management of behavioral and mental health disorders, and other integrative wellness initiatives. Pharmacy consultation services, including medication reconciliation and Medication Therapy Management, are provided primarily by pharmacists who specialize in neurology and/or psychiatry. In addition to Dr. Wagner, other faculty members of the Ernest Mario School of Pharmacy offer their services to the clinic. The clinic has funding to support a pharmacist being onsite one day a week; however, between the efforts of the various faculty members and the neuropsychiatry resident, onsite pharmacy services are provided most days of the week. As this is a collaborative practice model, pharmacists, nurses, and social workers assess and deliver care as a team. The majority of pharmacy interventions has been secondary to direct patient interaction and most often involve selection of the initial agent and dosage for treatment of a particular indication, providing counseling to the patients and care givers, and assisting the patient in obtaining medications and medical supplies, such as through enrollment in patient assistance programs and activation of savings cards and coupons.

In addition to participating in clinical pharmacy activities, a large component of the residency is focused on academia. The resident is required to develop and deliver didactic lectures at the Ernest Mario School of Pharmacy for Professional Year 3 students in the Neuropsychiatry Therapeutics and Advanced Neuropsychiatry Elective courses, with opportunities to teach classes in additional courses throughout the academic year. The resident also serves as a co-preceptor for those students who are on their Advanced Practice Experience Rotations. Each one of the aforementioned sites invites students in their last year of school at the

Ernest Mario School of Pharmacy to complete clerkship rotations onsite. In addition to serving as a mentor and resource for the students on rotation, the resident and faculty members lead topic discussions, assign projects, such as journal clubs, patient case presentations, seminars, and staff in-services, and supervise students as they make recommendations to providers and lead patient counseling sessions.

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Thank you again!

## Hanover Township Brown Bag Program

By Marlene Peterson, RPh

A Brown Bag Review is a unique opportunity for pharmacists to impart their knowledge to the general public in an individual manner in their municipality. The program is successfully underway in Hanover Township.

The patient, by appointment, is scheduled through the Township's Department of Health for a 30 to 45 minute consultation. The person bags up their medications (RX and OTC), supplements and herbals for the pharmacist's review. A form for listing them is sent to the patient in advance. A medication education session follows ensuring that the patient understands the indication of the medications they are taking, any potential drug interactions and side effects which they might encounter. Also, time of dosing, food interactions, duplication of therapy and other compliance issues are addressed. Questions about medication storage, expiration dates and manner of disposal are answered.

Personally, I initiated the Brown Bag Program by contacting the Health Department Officer. We set up a meeting with the Public Health Nurse. It turned out that they were as excited as I was in getting the program going. They created a flyer to be placed in public places, for example, the library, at senior citizen meetings and also in places of worship in the township. An article was published about the program in the local newspaper. The sessions are held twice a month in a dedicated room in the town hall.

The majority of patients who take advantage of a Brown Bag program are Senior Citizens. I stress at the start that all information is confidential and have them sign a consent form (and disclaimer). When they are asked if they have any questions about their medications I have found there are many instances of confusion and misunderstanding regarding their medication profile. At the

conclusion of the Brown Bag session, I present them with a proper list of their meds, doses and frequency and any recommendations that I suggest them to discuss with their pharmacist or physician. I give them a medical information card for their wallets. I also inquire about their current immunization needs.

At a recent Brown Bag interview a gentleman presented with 7 disease states and 17 medications. There were several drug-drug interactions and a number of compliance issues. I also counseled him on the proper use of his glucose meter and some diet modifications. Utilizing the information sources found on the Web and my 44 years of experience as a registered pharmacist, I have discovered that this is a wonderful way to help patients avail themselves to the services of a registered pharmacist in a relaxed setting. Too often, in the work setting, the pharmacist has very little time for counseling. The emphasis is on RX volume. It can become quite a challenge to answer questions, let alone, go over the entire medication profile.

I encourage you to begin a Brown Bag Program in your municipality. In my experience it was very well received by both the Township and the patients. While not only educating the patient, the program also promotes a better communications bridge between the person and the physician and pharmacist. Our recommendations are crucial and are of great benefit, especially in the senior population. We can make a difference! I don't charge for the service I perform and there is no charge to the patient, but I know how gratified I am that I have imparted useful information as to the understanding of the medications in such a positive way and have been instrumental in promoting good health to the participants.

"Brown Bag It". You'll be so pleased with the experience!



**Certificate Programs planned for July 13.**  
**Pharmacy-Based Immunization Delivery Certificate Training**  
**Pharmacists & Patient Centered Diabetes Care Certificate Training**



**Register online at [njpharmacists.org](http://njpharmacists.org). Click the Events tab, select Event Calendar, and scroll to July 13.**

**Space is limited, please register now!**

# The Impact of Pharmacists in Discharge Planning

The recognition of Pharmacists as integral members of interprofessional healthcare teams continues to increase. Pharmacists expertise in their ability to provide medication therapy management interventions in both the education of patients and providers of patient centered care relative to the proper use of medications has been proven to have a profound impact on overall patient medication compliance and hospital readmission rates.

According to **ASHP-APhA Medication Management in Care Transitions Best Practices\***, Pharmacists' patient counseling interventions at discharge and continued follow-up activities can reduce serious adverse drug events, use of emergency care, and hospital readmissions which have escalated into the billions of dollars.

In an effort to curtail readmission costs, many institutions across the healthcare continuum have begun to re-engineer their discharge planning processes incorporating the utilization of Pharmacists medication therapy management competencies at the time of patient discharge for discharge counseling and post discharge calls to physicians. This strategy has been proven to have a positive impact on increasing patient medication compliance, which in turn can reduce hospital readmission rates.

Many articles have been written to heighten an awareness of the financial impact of pharmacists in discharge planning and a study done by **Group Health Cooperative (Group Health) in Washington State, from September 2009 through February 2010** provides tangible statistics for consideration. Study findings docu-

ment the impact of assessment and reconciliation for patients post discharge by an ambulatory care clinical pharmacist relative to hospital readmission rates, financial savings, and medication discrepancies. Overall financial savings for Group Health per 100 patients who received medication reconciliation at an estimated \$35,000, translated to more than \$1,500,000 in savings annually. Of patients, 80% had at least one medication discrepancy upon discharge. \*\*

Such savings cannot be understated and should serve to be a point of reference for consideration in discussions with hospital administrators in their ongoing efforts to defray escalating hospital costs.

As the role of Pharmacists continues to evolve from a dispensing function to one of patient counseling, incorporating or redeploying Pharmacists to transitional care roles fostering engagement with patients and healthcare providers at the time of discharge planning to address medication discrepancies would ultimately serve the vested interests of both patients and healthcare providers

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**Booklet Interior.indd 1 2/21/13 9:04 PM ASHP-APhA Medication Management in Care Transitions Best Practices**

<http://japha.org/article.aspx?articleid=1656864>

## Contributors:

NJPhA Professional Affairs committee (Ruth Marietta, Sandra Moore, Barbara Rossi, Samy Ayoub, Ougua Osefoh)

## New Website Password Reminder

If you did not respond to the email notice to change your password in May, please reset your password to ensure you can access all the member features and program discounts.

Your user name is automatically set as the email address on file. Without a new password (you create it so you can remember it), the system will be unable to display member features and discounts.

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The screenshot shows the top navigation bar of the NJPhA website. It includes links for About, Membership, Events, Continuing Education, Political Action, Resources, and Contact Us. On the right side of the header, there is a search bar, a "Login / Register" button, and social media icons for Facebook, Twitter, and LinkedIn. Below the header, there is a circular logo for "NJPhA DONATE PAC".

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to all members in late June  
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First Vice President, Ruth Marietta  
Second Vice President, Ronald J. Mannino  
and Treasurer, John Colaizzi, Jr.**

**Voting deadline is Friday, July 11.**

**Don't leave money on the  
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## Management of Postpartum Depression

by Gregory J. Hughes, PharmD, BCPS, CGP and  
Linda Rosen, PharmD

### Learning Objectives:

After participating in this activity, the participant shall be able to:  
Pharmacist:

1. Identify symptoms and clinical characteristics of post partum depression.
2. Describe screening and diagnosis recommendations for post partum depression.
3. Describe the nonpharmacologic and pharmacologic management options for post partum depression.
4. Compare treatment options for patients with post partum depression who are breastfeeding.
5. Discuss the role of hormonal therapy in the treatment of post partum depression.

### Pharmacy Technician:

1. Identify medications used for the treatment of post partum depression.
2. Identify symptoms and clinical characteristics of post partum depression
3. Identify dosing ranges of medications used to treat post partum depression.
4. Describe nonpharmacologic options for the treatment of post partum depression.

UAN: 0136-0000-14-028-H04-P ; 0136-0000-14-028-H04-T

### Introduction

Postpartum depression is a common disorder following pregnancy that can have a significant impact to both the well-being of the mother and her new child. Postpartum depression can be divided into major and minor depression. While the exact incidence is unknown, it is estimated that 6.5 to 12.9 percent of mothers suffer from postpartum depression in the first year, of which 1 to 5.9 percent are considered major depression.<sup>1</sup> This is comparable to rates of major depression in the general population.<sup>2</sup>

### Clinical characteristics

Postpartum depression frequently begins within the first month following pregnancy but can be delayed for up to a year. The symptoms are similar to those of women who suffer from depression unrelated to pregnancy. These can include feelings of depressed mood, anxiety, sadness, guilt, anhedonia, irritability, anger, decreased energy, disrupted sleep, and problems with memory or concentration. Given the nature of infant care, some of these symptoms are likely to occur normally and may not be helpful in distinguishing between postpartum depression and normal changes (sleep disruptions, concentration impairment, and fatigue). Some women also will experience feelings of inadequacy or the inability to bond with their baby.<sup>3</sup>

While the pathogenesis for postpartum depression is not well understood, the combination of hormonal changes, genetic risk, and

the major life events of pregnancy and childbirth are all thought to play a role in its development.<sup>3</sup> Studies show a history of postpartum depression to be an important risk factor for recurrence.<sup>4</sup>

### Screening

The American College of Obstetricians and Gynecologists provide recommendations about screening for postpartum depression. While they do not recommend for or against universal screening, they do recognize the opportunity at this major life event to identify women who are at risk for postpartum depression and the potential benefit of providing support and treatment. Numerous screening tools have been developed and validated in various patient populations and can be administered at postpartum or well-child visits. These tools can quickly be completed by the patient and then scored by office staff.<sup>5</sup> One tool is the Edinburgh Postnatal Depression Scale which is a 10 item scale where each item is scored from zero to three points. A score of 10 or greater suggests possible depression. It is available for free and in a variety of languages.<sup>6</sup>

### Diagnosis

Diagnosis of postpartum depression by the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed., text revision requires meeting the criteria for a major depressive episode within four weeks of delivery.<sup>7</sup> This diagnosis requires five of the following symptoms lasting for at least two weeks: depressed mood (often with anxiety), anhedonia, appetite disturbance, sleep disturbance, physical agitation, fatigue, feelings of worthlessness, decreased concentration, or recurrent thoughts of death. These symptoms must be present most of the day, one of the symptoms must be a depressed mood or anhedonia, and for the postpartum depression to be considered major, there must also be an impairment of normal function.<sup>7</sup>

### Management

Management of postpartum depression involves multiple treatment options. First, a careful history, physical exam, and laboratory workup should be done to rule out organic causes for the patient's symptoms such as thyroid disorders, anemia, or other underlying psychiatric disorders. Laboratory testing should include thyroid-stimulating hormone to rule out hypothyroidism or hyperthyroidism since these can cause changes in mood. If a thyroid condition is found, it should be treated accordingly.<sup>8</sup> If the patient reports plans for suicide or actively harming her infant, urgent action should be taken. Likewise, if the patient is so functionally deficient that she is at risk of harming herself or her infant, rapid referral should take place for psychiatric care.

### Nonpharmacologic

Nonpharmacologic options for the management of depression include psychosocial and psychological interventions. These interventions have included peer support, cognitive behavioral therapy, and interpersonal psychotherapy. A Cochrane review found these interventions to be effective in reducing depressive symptoms.<sup>9</sup>

This may be an attractive option for women who would like to avoid pharmacologic options.

### Pharmacologic

Few studies have been conducted specifically on the pharmacotherapy of postpartum depression. In general, drug therapy is initiated similarly to major depressive disorder. There is no evidence that suggests one antidepressant is superior to another in treating postpartum depression. The selection of antidepressants is based primarily on the side effect profile of the drug and the extent of excretion into breast milk. (Table 1) Selective serotonin reuptake inhibitors (SSRIs) are considered first line because of their ease of administration and a more favorable adverse effect profile compared to tricyclic antidepressants (TCAs).<sup>10</sup> Alternative options are other medications used for depression such as serotonin norepinephrine reuptake inhibitors, bupropion, and mirtazapine. Patient's prior experience with antidepressants should also be considered before starting drug therapy. If a patient was successfully treated with an agent in the past, that agent should be considered first line unless a contraindication exists. Since postpartum women may be more sensitive to adverse effects of medications, it is reasonable to start at a low dose and slowly titrate up to the therapeutic dose.<sup>11</sup>

SSRIs act by inhibiting the presynaptic neuronal reuptake of serotonin resulting in enhanced serotonergic neurotransmission with little effect on reuptake of norepinephrine and dopamine. Similarly, TCAs inhibit presynaptic neuronal reuptake of norepinephrine and serotonin, but the potency and selectivity of inhibition varies greatly among agents. Because TCAs affect receptors in other systems such as cholinergic, neurologic, and cardiovascular systems, they are reported to have greater side effects compared to the more selective SSRIs.<sup>12</sup>

**Table 1<sup>8,13</sup> (Cont'd)**

Drug	Dose Range	Side Effects	Implications during breastfeeding
Escitalopram	10-20 mg/day		Infant risk has been demonstrated; escitalopram and its metabolite are excreted into breast milk; limited data shows infants received 3.9% & 1.7% of maternal dose of escitalopram and its metabolite respectively; adverse effects have been reported with citalopram.
<b>TCAs</b> Nortriptyline	50-150 mg/day	Sedation, weight gain, dry mouth, constipation, orthostatic hypotension, arrhythmias	Infant risk is minimal; infant serum levels generally undetectable; no reports of adverse events in infants.
Imipramine	50-150 mg/day		Imipramine and its active metabolite (desipramine) appear in breast milk at low concentrations; adverse effects not reported.
<b>SNRIs</b> Venlafaxine	75-300 mg /day	Headache, somnolence, dizziness, insomnia, nausea, tremor, dry mouth, sexual dysfunction, hypertension	Low serum levels of drug; metabolite usually measurable and levels can be as high as those in adults in some infants; drug level greater in breast milk than in maternal serum
Duloxetine	30-60 mg/day		Inadequate data for determining infant risk
<b>Other</b> Bupropion	200-450 mg/day	Dizziness, headache, dry mouth, sweating, tremor, agitation, seizures	Bupropion and its metabolites are excreted into human breast milk; potential for adverse effects in infant unknown.
Mirtazapine	15-45 mg/day	Somnolence, nausea, weight gain, dizziness	Inadequate data for determining infant risk; mirtazapine excreted in breast milk in modest amounts; infant serum concentrations low or undetectable

Abbreviations: SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; SNRI = serotonin norepinephrine reuptake inhibitor

**Table 1<sup>8,13</sup>**

Drug	Dose Range	Side Effects	Implications during breastfeeding
<b>SSRIs</b> Sertraline	50-200 mg/day	Dizziness, fatigue, headache, insomnia, sexual dysfunction, anorexia, diarrhea, nausea, dry mouth, tremors, somnolence	Infant risk is minimal; drug and weakly active metabolite generally not detectable in infants; no reports of adverse events
Paroxetine	20-50 mg/day		Infant risk is minimal; no active metabolite; levels not detectable in infants; no reports of adverse events
Citalopram	20-40 mg/day		Infant risk has been demonstrated; excessive somnolence, decreased feeding, colic, irritability, restlessness, and weight loss have been reported in breast-fed infants.
Fluoxetine	20-80 mg/day		Data is inconclusive for determining infant risk; fluoxetine and its active metabolite appear in breast milk; increased infant irritability has been reported.

Only 4 randomized controlled trials have been conducted with antidepressant drugs in postpartum depression. One placebo-controlled study involving 70 women with new onset postpartum depression compared immediate release paroxetine to placebo. Both groups improved significantly after 8 weeks of treatment with no statistical difference in the Hamilton Depression Rating Scale or the Inventory of Depressive Symptomatology (Self Report). However, the paroxetine group had a significantly higher rate of remission, compared to the placebo group (37% vs. 15%, odds ratio = 3.5, 95% CI = 1.1 to 11.5).<sup>14</sup> Almost half of the women in the study were breastfeeding but the effects in infants were not discussed. Another placebo-controlled trial compared fluoxetine, placebo, and cognitive behavioral therapy in 87 women with postpartum depression. The study involved 4 treatment arms. Women were randomized to either fluoxetine 20 mg daily or placebo with

each group further receiving either 1 or 6 counseling sessions. The fluoxetine groups had significant improvement compared to placebo. The combination of fluoxetine and 6 sessions of counseling had no benefit over either treatment alone.<sup>15</sup> Women who were breastfeeding, had depression for more than 2 years duration, or whose symptoms were severe enough to require close observation were excluded from this trial.

A double blinded comparative trial enrolled 109 women with postpartum depression. The women were randomized to receive either nortriptyline or sertraline with an escalating dose strategy over an 8 week period. Both the time to remission and the proportion of women in remission by week 8 were similar between groups. Approximately 45% of subjects were breastfeeding. No adverse effects were noted in breastfeeding infants, and infant serum levels were near or below measurable levels.<sup>16,17</sup> In another comparative study, 35 women with postpartum depression and concomitant anxiety were randomized to paroxetine monotherapy or paroxetine with 12 sessions of cognitive behavioral therapy for a 12 week trial. Both groups exhibited significant improvement in symptoms with no significant difference between groups. While there was no placebo arm of the study, 87.5% and 78.9% of women responded to monotherapy and combination, respectively. Approximately 50% of the women studied were breastfeeding but adverse effects and serum levels in infants were not reported.<sup>18</sup> Other small open trials and case reports have also suggested efficacy of antidepressants for postpartum depression.<sup>17</sup>

### **Antidepressants and Breastfeeding**

The Centers for Disease Control and Prevention National Immunization Survey reported breastfeeding rates from 2010 in the 2013 Breastfeeding Report Card. The survey reported 76.5% of infants were breastfed initially, 49% were partially breastfed at 6 months, 37.7% and 16.4% were breastfed exclusively at 3 and 6 months, respectively. These rates have been on the rise over the last decade.<sup>19</sup> Some studies have suggested that women with depression may be less likely to initiate or maintain breastfeeding, but the 2010 survey suggests that more than two-thirds of breastfeeding mothers with depression are likely to at least start breastfeeding. Therefore, the risk-benefit assessment of treating breastfeeding women with postpartum depression should include the risk to the infant of not treating the depression, the efficacy of antidepressant medication, and the risk of exposing the child to the antidepressant medication.<sup>20</sup>

All antidepressant medications pass into breast milk, therefore the potential for exposure to the infant exists with each medication. Although observational reports suggest a lack of short-term adverse effects in infants with many antidepressants, the long-term risk has not been evaluated.<sup>17</sup> See Table 1 for more information on breastfeeding outcomes of individual agents.

### **TCAs**

The majority of data on infant serum levels with TCAs includes nortriptyline and imipramine. In most cases the serum levels of these drugs are undetectable and no adverse effects were reported. Because of its sedating properties and its metabolite's long half-life, doxepin has been associated with respiratory depression and should be avoided when breastfeeding. TCAs may be considered first line treatments if the mother has been successfully treated in the past and there are no other contraindications, such as suicidality.<sup>21</sup>

### **SSRIs**

During the first few days of treatment with SSRIs, patients may experience adverse effects due to rapidly increased serotonin levels such as insomnia, sexual dysfunction, and gastrointestinal disturbances. These effects are generally mild and resolve with desensitization of post-synaptic receptors. For this reason, it has been recommended to start with a low dose and titrate up.<sup>16</sup>

Recommendations for using antidepressants in breastfeeding mothers include the following:

- 1) The choice of specific treatment should be based on a personalized risk versus benefit assessment, including the severity of maternal symptoms.
- 2) Patients should be given all available information regarding their treatment options in order to make informed decisions about their care.
- 3) Nonpharmacologic treatments should be considered first line for mild to moderate postpartum depression.
- 4) Antidepressants should be considered (either alone or in combination with cognitive behavioral therapy) for women with moderate to severe symptoms or not responding to psychotherapy.
- 5) Choice of antidepressants should be based on the patient's previous response.
- 6) If the woman is afflicted with her first lifetime episode of depression, sertraline or paroxetine should be considered first line agents.
- 7) Start the antidepressant at the lowest effective dose and titrate up slowly.
- 8) Single drug therapy is preferred over combination drug therapy.
- 9) Mothers and infants should be clinically monitored for adverse effects.
- 10) Infant serum levels are not routinely recommended.<sup>21</sup>

### **Hormonal therapy**

Studies suggest that fluctuations in estrogen and progesterone play a role in the development of postpartum depression in a subgroup of women. This theory is supported by the 2-3.5 fold increased risk for hospitalization due to depression in the first 5 months after childbirth, the 2-5 fold increased risk for depression symptoms in perimenopausal women versus premenopausal women, and the 1.7 fold increased risk for depression in women of childbearing age compared to men. Women who are susceptible to mood changes during reproductive transitions, such as premenstrual dysphoric disorder, may be at greater risk for future reproductive hormone related mood disorders as well.<sup>22</sup>

One study randomized 61 non-breastfeeding women with severe depressive symptoms to 6 months of treatment with either placebo or high dose transdermal 17beta-estradiol. Patients were assessed monthly for symptom improvement based on Edinburgh Postnatal Depression Scale scores. At 3 months, 80% of the estradiol group scored below 14 on the Edinburgh Postnatal Depression Scale compared to 31% of the placebo group indicating a possible role for estradiol. By 6 months, both groups had reduced scores but only the scores for the patients in the estradiol group were consistent with symptom remission.<sup>23</sup>

An open label study treated 23 women with sublingual 17beta-estradiol for 8 weeks. The treatment effect was assessed using a

clinician-rated depression symptom scale, the Montgomery-Asberg Depression Rating Scale. At baseline, all patients were severely depressed and had low serum estradiol levels. Within one week of treatment, 50% of patients had symptom score reductions and 83% were in remission after 2 weeks.<sup>24</sup>

While these studies suggest the efficacy of estradiol in the treatment of postpartum depression, it is important to keep in mind their limitations. In the randomized trial, almost half of the women in each arm were concurrently treated with antidepressants, making it difficult to distinguish estradiol's place in therapy (monotherapy vs. augmentation of antidepressant effects). The trial also used the self-reported scale for measuring symptom resolution rather than a clinical interview assessment. The exclusion of breastfeeding women and those with mild-moderate symptoms limits the generalizability of the study results. Both studies included women who presented for treatment up to 12-18 months postpartum. The theoretical contribution of estrogen withdrawal at delivery to the risk of developing postpartum depression is the primary rationale for estradiol treatment. However, this time frame is far longer than this theorized withdrawal period. Whether earlier treatment with high dose estradiol will lead to improved rates of remission still remains to be studied. Further research is needed to confirm these findings and to assess the safety of estradiol in postpartum women, such as decreased milk production in lactating women or thromboembolism.<sup>22</sup>

In contrast, progesterone has not been proven effective in the treatment of postpartum depression. Review of the literature does not produce any vigorous primary research in the effectiveness of progesterone in postpartum mood disorders.<sup>25</sup> The safety of progesterone in postpartum women will need further evaluation as well. One study of long-acting norethisterone enanthate given within 48 hours of delivery resulted in an increased risk of developing postpartum depression and caused suppression of endogenous ovarian hormone secretion.<sup>26</sup>

## Conclusion

Postpartum depression is a common disorder experienced by new mothers that can have important consequences for the mother and her infant. Antidepressant medications and nonpharmacologic cognitive therapy are currently the cornerstones of treatment. The decision on how to treat the depression should be a joint undertaking which considers patient preference, side effects, breastfeeding, cost, and prior experience with pharmacologic agents.

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UAN: 0136-0000-14-028-H04-P; 0136-0000-14-028-H04-T Management of Postpartum Depression

## Questions

1. Which statement is true regarding the clinical characteristics of post partum depression?
  - a. symptoms frequently begin within the first few months following pregnancy
  - b. symptoms can help distinguish between post partum depression and normal changes associated with infant care
  - c. symptoms are significantly different from symptoms of depression unrelated to pregnancy
2. Which statement is true regarding screening for post partum depression?
  - a. the American College of Obstetricians and Gynecologists recommends universal screening for everyone who has given birth
  - b. although numerous screening tools are available, none have been validated in this population
  - c. screening tools can be completed by the patient and scored by office staff
  - d. a Edinburgh Postnatal Depression Scale result of 7 is suggestive of post partum depression
3. According to the DSM4, the diagnosis of post partum depression specifies that symptoms last for at least
  - a. 48 hours
  - b. 2 weeks
  - c. 3 months
  - d. 9 months
4. In managing post partum depression, urgent action should be taken if the patient
  - a. has significant weight loss
  - b. misses post partum doctor's appointments
  - c. reports plans of harming her infant
  - d. complains of insomnia
5. Non pharmacologic management of post partum depression may include
  - a. electroconvulsive therapy, SSRIs, and peer support
  - b. cognitive behavioral therapy, peer support, and interpersonal psychotherapy
  - c. group therapy, isolation, and sertraline
  - d. breast feeding, cognitive behavioral therapy, and electroconvulsive therapy

## CE Assessment Answers

Passing Score is 70% or above

Please circle your answers (one answer per question)

- |      |   |   |   |       |   |   |   |
|------|---|---|---|-------|---|---|---|
| 1. A | B | C | D | 6. A  | B | C | D |
| 2. A | B | C | D | 7. A  | B | C | D |
| 3. A | B | C | D | 8. A  | B | C | D |
| 4. A | B | C | D | 9. A  | B | C | D |
| 5. A | B | C | D | 10. A | B | C | D |

## Program Evaluation – Must be completed for credit

Please rate the following items on a scale from 1 (poor) to 4 (excellent).

- |                                   |   |   |   |   |
|-----------------------------------|---|---|---|---|
| 1. Overall quality of the article | 1 | 2 | 3 | 4 |
| 2. Relevance to pharmacy practice | 1 | 2 | 3 | 4 |
| 3. Value of the content           | 1 | 2 | 3 | 4 |

Please answer if you agree or disagree

4. The program met the stated learning objectives:  Agree  Disagree

## Impact of the Activity

5. The information presented (check all that applies):

- Reinforced my current practice/treatment habits
- Will improve my practice/patient outcomes
- Provided new ideas or information I expect to use
- Adds to my knowledge

6. Will the information presented cause you to make any changes in how you do your job?  Yes  No

7. How committed are you to making these changes?  
(Not committed) 1 2 3 4 (Very committed)

6. Drug therapy for post partum depression is initiated similarly to drug therapy for
  - a. peripheral neuropathy
  - b. bipolar disorder
  - c. acute panic attacks
  - d. major depressive disorder
7. Selection of antidepressant therapy for post partum depression is based primarily on
  - a. side effect profile and maximum daily dose
  - b. side effect profile and prior response to medication
  - c. maximum daily dose and liver toxicity
  - d. liver toxicity and extent of excretion into breast milk
8. Which statement is true regarding first line therapy for post partum depression?
  - a. TCAs are first line in patients who are suicidal
  - b. TCAs are first line because they have few side effects
  - c. SSRIs are first line in patients who previously responded to TCAs
  - d. SSRIs are first line because of their lower risk of adverse effects
9. According to Table 1, which statement is true regarding the risk to the infants of mothers who took antidepressants while breastfeeding?
  - a. levels of the active metabolite of paroxetine are detectable in the infant
  - b. weight loss has been reported in breast fed infants whose mothers took citalopram
  - c. infant serum levels of nortriptyline are high in breast fed infants whose mothers took nortriptyline
  - d. drug levels of venlafaxine in breast milk are similar to the levels in the maternal serum
10. Which of the following medications is a hormonal therapy that has been used to successfully treat post partum depression?
  - a. 17 beta-estradiol
  - b. progesterone
  - c. bupropion
  - d. norethisterone enanthate

8. Do you feel future activities on this subject matter are necessary and/or important?  Yes  No

## Follow-Up

As part of our ongoing quality-improvement effort, we would like to be able to contact you in the event we conduct a follow-up survey to assess the impact of our educational interventions on professional practice. Are you willing to participate in such a survey?  Yes  No

This lesson is a knowledge-based CE activity and is targeted to pharmacists and pharmacy technicians. This program has been approved for 1 contact hour of continuing education credit (0.1 CEU). To receive continuing education credit, please provide the following information:

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# continuing education for pharmacists

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## Therapeutic Actions and the Genetic Code: Examples of the Application of Pharmacogenetics

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Dr. David Kisor and Ms. Angela Smith have no relevant financial relationships to disclose.

**Goal.** The goal of this lesson is to provide information on how differences in genetics can affect patient response to drugs, causing both therapeutic effects and adverse reactions, to help pharmacists provide better medication therapy management.

**Objectives.** At the completion of this activity, the participant will be able to:

1. demonstrate an understanding of pharmacogenetics and its application to pharmacy practice;
2. recognize variations in genes and the nomenclature used to identify variant alleles;
3. identify variation in alleles, diplotypes and metabolic phenotypes which can result in altered therapeutic response and adverse effects in patients; and
4. list examples of drug-gene interactions and interpret how these apply to patients in specific cases.

### Introduction

The term pharmacogenetics (PGt) refers to differences in a given gene that can affect an individual's response to drugs. The variation in metabolism due to genetics can alter both the therapeutic effect of medications, as well as cause adverse effects. Drug-gene interactions are similar to drug-drug interactions, putting pharmacists

in a unique position to apply their extensive drug knowledge and proficiently fill a new gap in medication management.

DNA is composed of a sequence of nucleotides (the triphosphates of adenine [A], cytosine [C], guanine [G], and thymine [T]), and serves as a "production manual" for the assembly of proteins. In relation to drugs, genes of interest ("pharmacogenetic genes") are the segments of DNA which code for receptors, transporters, and metabolizing enzymes. There are approximately 25,000 genes in the human genome, i.e., the entirety of DNA, with variations resulting in differences in pharmacodynamics (PD), or how individuals respond to a drug, and pharmacokinetics (PK), or how individuals "handle" a drug with respect to absorption, distribution, metabolism and excretion (ADME).

A variant form of a gene, called an *allele*, may result in altered drug response, due to altered PD or as a result of altered ADME. The most common variation in a gene is the single nucleotide polymorphism or SNP (pronounced "snip") which is the case where a single nucleotide is replaced in the gene DNA sequence by another nucleotide, such as T replacing C. For instance, the C in position 634 of a gene being replaced by T would be noted as 634C>T. As a SNP produces a variant allele, the variant form of the gene is given a specific designation to differentiate it from the "common" form. The variant

form may result in altered protein function.

With reference to the cytochrome P450 (CYP) enzyme family, responsible for metabolizing many drugs, a "star" nomenclature has been adopted, where the most common form of a gene is typically termed the \*1 form and variant forms are designated otherwise, such as \*2, \*3, and so on. It should be noted that a given "\*" variant for one gene, such as \*17, does not necessarily have the same meaning as a \*17 variant for a different gene. For instance, the \*17 form of the *CYP2C19* gene is a "gain-of-function" form resulting in increased drug metabolism by *CYP2C19*, whereas the \*17 form of the *CYP2D6* gene is a "reduced-function" form resulting in decreased drug metabolism by *CYP2D6*.

Different alleles can affect protein function and, as in the case of the CYP enzyme family, this can lead to variability in drug metabolism. Some genetic effects are more drastic than others and, in the more extreme cases, genetic testing may make the difference between therapeutic failure and success, or safety and toxicity.

As data supporting the use of genetic testing in drug therapy decision-making accrues, more and more pharmacies are offering services that integrate pharmacogenetics into medication therapy management (MTM) programs. Currently, pharmacogenetic-based dosing guidelines have been pub-

lished for 10 gene-drug pairs: thiopurine methyltransferase (*TPMT*)-thiopurines; cytochrome P450 2C19 (*CYP2C19*)-clopidogrel; *CYP2C9* and vitamin K epoxide reductase subunit 1 (*VKORC1*)-warfarin; *CYP2D6*-codeine; human leukocyte antigen B (*HLA-B*)-abacavir; solute carrier organic anion transporter 1B1 (*SLCO1B1*)-simvastatin; *HLA-B*-allopurinol; *CYP2D6* and *CYP2C19*-tricyclic antidepressants (TCAs); *HLAB*-carbamazepine; and dihydropyrimidine dehydrogenase (*DPYD*)-5-fluorouracil and capecitabine. Additionally, another five guidelines are under development.

Guidelines are available on the pharmacogenomics knowledgebase website ([www.pharmgkb.org](http://www.pharmgkb.org)) and are available as open access publications in *Clinical Pharmacology and Therapeutics*.

Relating a patient's drug response to genetics defines PGt. Genetic factors represent the underlying variability in response to a drug, notwithstanding environmental factors, diet, pathophysiology, concomitant drug use, and other factors that introduce variability. Table 1 provides examples of drug-gene interactions and the potential outcome of each interaction. Four specific case examples of the application of pharmacogenetics will be presented.

### ***CYP2D6*-Codeine**

Cytochrome P450 2D6 (*CYP2D6*) is a major drug metabolizing enzyme, responsible for metabolizing approximately 20 percent of drugs. There are more than 80 different alleles of the *CYP2D6* gene, which can result in a spectrum of *CYP2D6* enzyme activity. As an individual receives genetic information from each parent, the combination of alleles (called a *diploidotype*) will impart a certain level of enzyme activity relative to drug metabolism. Each allele inherited by an individual contributes to the phenotype of enzyme activity that is expressed and allows individuals to be classified by a "metabolism phenotype," such as *ultrarapid me-*

**Table 1**  
**Examples of drug-gene interactions and potential outcomes**

Gene	Drug	Variant Allele (SNP) <sup>a</sup>	Effect on Protein <sup>b</sup>	Effect on PK/PD <sup>c</sup>	Potential Outcome
<i>HLA-B</i>	carbamazepine	15:02	HLA-B-altered protein structure	T-cell mediated immune response	Stevens-Johnson syndrome; toxic epidermal necrolysis
<i>CYP2C19</i>	clopidogrel	*17 (C>T) rs12248560 <sup>d</sup>	increased CYP2C19 enzyme activity	increased clearance (conversion) <sup>e</sup>	increased clopidogrel effect; bleeding
<i>CYP2D6</i>	codeine	*3 A deleted rs35742686	nonfunctional CYP2D6 enzyme	decreased clearance (conversion) <sup>f</sup>	decreased codeine effect; lack of pain relief
<i>CYP2C9</i>	warfarin	*2 (C>T) rs1799853	decreased CYP2C9 enzyme activity	decreased clearance	increased warfarin effect; bleeding

<sup>a</sup>SNP = single nucleotide polymorphism where one DNA base (adenine (A), cytosine (C), guanine (G), and thymine (T)) replaces another (e.g., such as T replacing C; C>T). <sup>b</sup>Pharmacogenetic proteins include receptors, drug transporters, and drug metabolizing enzymes.

<sup>c</sup>PK/PD = pharmacokinetics/pharmacodynamics. <sup>d</sup>rs number = a specific and consistent identifier of the SNP as found in the SNP database (dbSNP) of the National Center for Biotechnology Information. <sup>e</sup>The increased clearance of clopidogrel results in greater conversion to the active metabolite. <sup>f</sup>The decreased clearance of codeine results in less conversion to morphine, which is largely responsible for the analgesic effects of codeine.

*tabolizer* (UM) or *poor metabolizer* (PM). The classification of an individual by metabolism phenotype has shown to be of consequence when considering the use of codeine. **Case Example #1** describes one of the extremes of genetic influence on drug response.

This case example illustrates

a lack of drug effectiveness. Neither JS nor his brother underwent simple pharmacogenetic testing relative to *CYP2D6* prior to receiving the codeine-containing product. Subsequent testing through a university medical center study showed that JS and his brother were in fact poor metabolizers,

### **Case Example #1**

JS, a 19 y.o. healthy Caucasian male, is a body shop mechanic. JS visited the nearby university medical center emergency department (ED) after slicing his hand on a piece of sheet metal. Following suturing (18 stitches), the hand was bandaged and wrapped. JS was in pain and was complaining that his hand was "throbbing." He was given acetaminophen/codeine phosphate (300 mg/30 mg) in the ED and provided a prescription for a 72-hour period with the instructions to take 1 to 2 tablets every 4 to 6 hours as needed for pain. At the pharmacy, he asked if this was the same as Tylenol #3 because his younger brother had some prescribed for him after he had his tonsils removed. JS explained that the Tylenol #3 did not help his brother at all, so they "have plenty at home." The pharmacist explained that prescriptions are for specific individuals, and JS agreed to get the prescription filled for him and not use what was left from his brother's prescription. The pharmacist also told JS to monitor if the pain medication was working. At 36 hours, JS was still experiencing severe throbbing pain and called the pharmacy. The pharmacist discussed the situation with JS' family physician, who prescribed an alternative analgesic, which was used by JS with success. In discussion with JS' family physician, the pharmacist explained that the lack of efficacy of the acetaminophen/codeine combination may have a genetic basis, as neither JS nor his younger brother experienced pain relief with the codeine containing product.

each with a \*3/\*4 diplotype (combination of *CYP2D6* gene variants inherited from each parent). Having a diplotype that produced nonfunctional *CYP2D6* enzymes, neither JS nor his brother had the metabolic capacity to convert codeine (a prodrug) to morphine (the active drug), which is largely responsible for the analgesia produced with acetaminophen/codeine use.

The other extreme of *CYP2D6* enzyme activity, where excessive amounts of morphine are formed following codeine administration, is seen in individuals who are ultrarapid metabolizers. These individuals are at risk of morphine toxicity due to very efficient conversion of codeine. Additionally, infants who were breastfeeding have tragically died of morphine overdose because their mothers were UMs receiving codeine-containing products. Here, the infants received morphine that was passed onto them in the breast milk.

The Clinical Pharmacogenetics Implementation Consortium (CPIC) pharmacogenetic-based dosing guidelines suggest avoiding codeine use in UM and PM individuals due to the potential for toxicity and lack of efficacy, respectively. Finally, in early 2013, the Food and Drug Administration issued a black box warning for the labeling of codeine-containing products, as well as a contraindication to the use of codeine-containing products in children following tonsillectomy and/or adenoidectomy. The aim of this labeling is to try and prevent opioid toxicity and death due to codeine use in children who may be UMs. The therapeutic action, based on an individual's genetics, would be to use an alternative opioid or a non-opioid analgesic.

### ***HLA-B-Carbamazepine***

The human leukocyte antigen (*HLA*) gene family is responsible for the coding of the *HLA* complex, a group of proteins which guide the immune system in identifying "foreign" cells. Individuals with the gene variant *HLA-B\*15:02* are at increased risk of a T-cell-mediated

immune response, resulting in the potentially life-threatening skin disease of Stevens-Johnson syndrome (SJS; also called erythema multiforme majus) or toxic epidermal necrolysis (TEN). SJS can be expressed as a mild form with the patient experiencing fever, itching, and malaise. Additionally, lesions (macular, papular, hive-like, with or without blisters) may be found symmetrically on the trunk and on upper and lower extremities. The severe form of SJS includes less than 10 percent of the patient's body surface area (BSA) being necrotic skin. When necrotic lesions extend beyond 30 percent of the BSA, the diagnosis of TEN is made. In addition to mucosa and skin involvement in SJS and TEN, vital organs can also be affected and severe forms result in mortality rates up to 40 percent, most often due to sepsis.

It is thought that carbamazepine hypersensitivity is the result of the drug's metabolites altering cellular proteins. The protein alteration results in the immune system identifying cells as "foreign" and elicits a T-cell mediated immune response, culminating in SJS or TEN. Individuals with the variant *HLA-B\*15:02* are at increased risk of SJS and TEN when taking carbamazepine. **Case Example #2** illustrates the *HLA-B*-carbamazepine interaction.

### **Case Example #2**

YL is a 17 y.o. Chinese male who is participating in a cultural exchange program with the United States. YL lives with his host family in Southwest Ohio. While attending a college baseball game, YL experiences a generalized tonic-clonic seizure. YL's airway and head are protected, and the seizure ends after approximately 90 seconds. YL is evaluated and transported by ambulance to the medical center emergency department. There is no documentation that YL has a seizure history, and it was never mentioned by YL or the exchange agency. In discussing treatment options, the pharmacist points out that the Asian population and, in particular, individuals of Han Chinese descent have been shown to have an increased risk of SJS and TEN related to the interaction of *HLA-B\*15:02* with carbamazepine. With this in mind, alternative treatment options are considered.

The presence of one or two copies (one from each parent) of the variant *HLA-B\*15:02* allele imparts an increased risk of developing SJS or TEN in patients who are to receive carbamazepine. Table 2 presents the frequencies of *HLA-B\*15:02* in U.S. Asian populations. It should be noted that oxcarbazepine has also been shown to cause skin reactions in *HLA-B\*15:02* positive individuals. The therapeutic action here, based on

**Table 2**  
**The frequency of occurrence of *HLA-B\*15:02* in U.S. Asian populations compared to the reference population of Han Chinese<sup>a</sup>**

Population	Frequency (%) of occurrence of <i>HLA-B*15:02</i> <sup>b</sup>	Total # of individuals tested for <i>HLA-B*15:02</i>	Approximate # of individuals testing "positive" for <i>HLA-B*15:02</i>
Han Chinese <sup>c</sup>	13	101	13
U.S. Asian population 1	5	358	18
U.S. Asian population 2	4	1772	71

<sup>a</sup>Adapted from [allelefrequencies.net](http://allelefrequencies.net) with the noted Han Chinese frequency for reference

<sup>b</sup>Rounded to approximate whole number

<sup>c</sup>Example Han population (Yunnan Province)

an individual's genetics, would be to use an alternative antiepileptic therapy that does not increase the risk of SJS or TEN in *HLA-B\*15:02* positive individuals. The CPIC has recently published guidelines related to the *HLA-B\*15:02*-carbamazepine interaction.

### ***CYP2D6/CYP2C19-Tricyclic Antidepressants***

Many drugs are metabolized by multiple cytochrome P450 enzymes such that specific isozyme (e.g., *CYP2D6*, *CYP2C19*) genotypes can influence the overall elimination (clearance) of a given substrate drug. Variant forms of the *CYP2D6* and *CYP2C19* genes produce increased enzyme function. Examples include multiple copies of functional variants as seen in *CYP2D6* UM; increased transcription (more RNA is transcribed from DNA, which results in increased production of the enzyme) as exhibited by the *CYP2C19\*17* gene variant. Conversely, *CYP2D6* and *CYP2C19* alleles can also produce reduced-function or loss-of-function enzymes. For example, *CYP2D6\*4* and *CYP2C19\*2* are non-functional. The combinations of genetic variability relative to both *CYP2D6* and *CYP2C19* can influence the ADME and overall concentration versus time profile of substrate drugs and metabolites. Some examples of substrates for *CYP2D6* and *CYP2C19* include amitriptyline, nortriptyline, imipramine, and other tricyclic antidepressants.

Amitriptyline is metabolized to nortriptyline and imipramine is metabolized to desipramine via *CYP2C19*. Amitriptyline and nortriptyline are metabolized by *CYP2D6* to their respective 10-hydroxy metabolites, whereas imipramine and desipramine, also via *CYP2D6*, are metabolized to their 2-hydroxy metabolites. The hydroxy metabolites are less active than their parent compounds. The overall metabolism of these drugs requires multiple steps, and at each step a different enzyme is introduced into the process. With multiple alleles existing for each

enzyme, this adds a layer of complication and can allow for increased variation in drug metabolism.

As mentioned earlier, there are numerous variant alleles of the *CYP2D6* gene that contribute to various metabolism phenotypes. With respect to *CYP2C19*, there are 28 confirmed variant alleles, with the \*2, \*3, and \*17 alleles being most commonly implicated in altered drug metabolism (Table 3). An individual with one "normal" copy of the gene and one copy of either the \*2 or \*3 alleles would be considered an intermediate metabolizer (IM), whereas an individual with two copies of the \*2 or \*3 alleles would be considered a PM. A \*2/\*3 individual would also be a PM, as both of the alleles are loss-of-function forms of the gene. The \*17 form is considered a gain-of-function allele and individuals with the common form (\*1) and the \*17 allele, or two copies of the \*17 allele, would be considered UM. Certainly the combination of *CYP2D6* and *CYP2C19* variant genes can be expected to impact drug metabolism, thus influencing an individual's response to tricyclic antidepressants including amitriptyline and imipramine. Consider Case Example #3.

Recall that amitriptyline is converted to nortriptyline via *CYP2C19*. In this case, the patient is an IM, which is likely the cause of elevated amitriptyline concentrations. Additionally, the patient is a *CYP2D6* PM indicating decreased conversion of both amitriptyline and nortriptyline to their respective 10-hydroxy metabolites. The patient's genetic coding for decreased metabolism relative to the *CYP2D6* and *CYP2C19* pathways is likely responsible for the adverse effect noted in the above case. The interactions of *CYP2D6* and *CYP2C19* with tricyclic antidepressants have been evaluated and discussed. With two genes playing an important role in the metabolism of TCAs and both having many variants, predicting potential pharmacokinetic effects and the response to a given TCA can be difficult. The

### **Case Example #3**

JD is a 51 y.o. African American male who presents to his family physician complaining of loss of appetite, fatigue, and apathy. He states he has been having difficulty at work and just "doesn't sleep well." He also states that he has been "irritable" and "quick to jump at people." JD adds that he has been feeling more and more frustrated with day to day life. He confides that he started feeling this way over the past two months after the death of his father, whom he was very close to. JD's physician makes an initial diagnosis of depression. Being older, the physician is most familiar with the use of the tricyclic antidepressant agents and starts JD on amitriptyline. JD receives 25 mg of amitriptyline BID. After two weeks, JD contacts his physician, complaining of confusion, lack of concentration and vomiting. JD is directed to be taken by his wife to the local hospital emergency department. At the ED, JD is examined, with the EKG showing a prolonged QRS complex with a right bundle branch block. While JD is receiving a relatively low dose of amitriptyline, the diagnosis of amitriptyline toxicity is made. As JD brought his vial of amitriptyline with him, a "pill count" indicates that JD has been following the administration directions. The ED physician calls the pharmacy to check on the generic form of the amitriptyline to see if it is the correct strength. A pharmacist confirms the strength of the tablets and suggests that pharmacogenetic testing be performed to identify the patient's metabolic phenotype relative to *CYP2D6* and *CYP2C19*. JD provides a cheek swab sample for DNA analysis. The amitriptyline is held and JD is monitored. JD is discharged from the ED with instructions to see his family physician for follow-up. After five days the pharmacogenetic test results are available, indicating that JD is a *CYP2D6* poor metabolizer with a \*4/\*4 diplotype and *CYP2C19* intermediate metabolizer with a \*1/\*2 diplotype. These results explain the adverse reactions being related to amitriptyline overdose, here due to decreased metabolism as compared to the actual dose being considered too high. JD is switched to a selective serotonin reuptake inhibitor (SSRI) and responds well to treatment.

**Table 3**  
**Examples of CYP2C19 alleles, diplotypes, and metabolic phenotypes**

Functionality	Example Diplotype <sup>a</sup>	Metabolic Phenotype
Fully functional: *1 (wild type)	*1/*2	IM <sup>b</sup>
Loss-of-function: *2, *3, others	*2/*2	PM <sup>c</sup>
Gain-of-function: *17	*2/*17 *1/*1 *1/*17	IM EM <sup>d</sup> UM <sup>e</sup>

<sup>a</sup>Combination of alleles (one from each parent)  
<sup>b</sup>Intermediate metabolizer  
<sup>c</sup>Poor metabolizer  
<sup>d</sup>Extensive metabolizer  
<sup>e</sup>Ultrarapid metabolizer

recently published CPIC guidelines can help with the interpretation of such information. Based on the individual's genetics, the therapeutic action would be to use an alternative to a TCA for treatment of depression.

### CYP2C19-Clopidogrel

As previously mentioned, CYP2C19 is a drug metabolizing enzyme which is responsible for metabolizing between 5 and 10 percent of drugs. The CYP2C19 gene has been mostly discussed relative to the drug clopidogrel when considering conversion of this prodrug to its active form. The \*1 form is related to normal metabolism, and is also commonly referred to as *extensive metabolism*. The \*2 and \*3 alleles, as present in heterozygous individuals (having two different alleles i.e., \*1/\*2, \*1/\*3) or homozygous individuals (having two of the same alleles i.e., \*2/\*2, \*3/\*3) result in decreased conversion of clopidogrel to its active form. This decreased conversion has been related to increased cardiovascular risk factors in patients having undergone coronary artery stent placement during percutaneous coronary intervention for treatment of acute coronary syndrome (ACS). In 2010, FDA issued a black box warning for clopidogrel stating that it may not be effective for patients with reduced CYP2C19 metabolizing

capability. The \*17 allele is associated with increased conversion of clopidogrel to its active metabolite, which puts the patient at increased risk for bleeding. **Case Example #4** presents an example of a CYP2C19-clopidogrel interaction.

Each CYP2C19 gene can be categorized as a gain-of-function, normal function or loss-of-function allele. The combination of two alleles (one from each parent) results in the following expected "metabolizer" phenotypes: ultrarapid, extensive (normal), intermediate or poor (Table 4). The genotypes and expected metabolizer phenotypes have been evaluated relative to clopidogrel use as described by CPIC. The therapeutic action here,

### Case Example #4

MR is a 52 y.o. Caucasian male. MR is an outpatient visiting the ambulatory care pharmacy to have his prescription for prasugrel filled. He explains that he is "very keen" about taking his prasugrel following the placement of two "tubes" in his "heart arteries." MR was previously diagnosed with ACS. He had gone to the ED after experiencing dizziness and chest pain. He had two stents placed to prevent coronary artery thrombosis and the consequences of a clot. MR was given a 60 mg loading dose of prasugrel and a prescription with the instructions to take one 10 mg tablet daily. His only other medication is atorvastatin 20 mg daily, being used for hyperlipidemia that was diagnosed five years ago. MR does not have prescription coverage as part of his healthcare insurance and is "shocked" at the price of prasugrel. He asks the pharmacist if there is an alternative drug he can take. The pharmacist suggests MR undergo pharmacogenetic testing, which is more expensive than a single prasugrel prescription, but in the long run will likely save MR a great deal of money. MR agrees to have a pharmacogenetic test done with the results indicating that he is an extensive metabolizer with a CYP2C19 \*1/\*1 diplotype. The pharmacist contacts MR's family physician and the prasugrel is changed to clopidogrel 75 mg daily.

**Table 4**  
**CYP2C19 alleles as related to expected metabolizer phenotypes**

Gene from second parent		Gene from first parent		
		gain-of-function allele	normal function allele	loss-of-function allele
gain-of-function allele		UM <sup>a</sup>	UM	IM <sup>b</sup>
normal function allele		UM	EM <sup>c</sup>	IM
loss-of-function allele		IM	IM	PM <sup>d</sup>
<sup>a</sup> Ultrarapid metabolizer		<sup>b</sup> Intermediate metabolizer		
<sup>c</sup> Extensive metabolizer		<sup>d</sup> Poor metabolizer		

based on the individual's genetics, would be to use clopidogrel as a less expensive alternative to prasugrel.

## Summary

Testing of an individual's pharmacogenetics is becoming more widely available and published dosing guidelines support its application in many pharmacy settings. Additionally, it is likely within the next five to 10 years that preemptive genetic testing, including partial or whole-genome (all genes) testing,

will become a reality. Having the data available at the point of care will aid in the application of PGt.

Drug-gene interactions as described by the examples above can be thought of in a similar way to drug-drug interactions. The expertise of pharmacists calls for the profession to embrace PGt as an integral component of medication therapy management. Pharmacists need to be educated about PGt and should expect to educate other healthcare providers and patients regarding drug-gene interactions.

*The authors, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.*

This lesson is an application-based CE activity and is targeted to pharmacists in all practice settings.

**Program 0129-0000-13-012-H01-P**

Release date: 12-15-13

Expiration date: 12-15-16

CE Hours: 1.5 (0.15 CEU)

The Ohio Pharmacists Foundation Inc. is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.



Therapeutic Actions and the Genetic Code CE exam on the following page

# NJPhA ANNUAL CONVENTION 2014 POSTER CALL

Join the second annual Poster Session on September 20, 2014 @The Berkeley Hotel in Asbury Park, NJ.

**Encores welcome!**

**Logistics:** Posters set up begins Friday, September 19<sup>th</sup> in the afternoon and must be completed by 7:30 AM on Saturday, September 20<sup>th</sup>.\* The formal poster session (required presentation) is scheduled for Saturday, September 20<sup>th</sup> from 2:45 - 3:15 PM. Posters are on display throughout the day and you are welcome to be available by your poster before the allotted time. Posters may be removed after the session or as late as 7:30 AM the following (Sunday) morning.

**Submission Deadline & Details:** Poster applications will be accepted through July 30, 2014. Accepted Poster applicants will be notified approximately one month prior to the Convention.

Register online at <http://njpharmacists.org/events/annual-convention> Click on the Get Details button under the Convention 2014 Poster call heading on the right.



To submit, complete the form and email using contact information below.

**Poster Presenters are invited to Sessions, Refreshments & Meals**

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[njpharmacist.org](http://njpharmacist.org)

## continuing education quiz

## Therapeutic Actions and the Genetic Code: Examples of the Application of Pharmacogenetics

- All of the following are components of DNA EXCEPT:
    - adenine.
    - cytosine.
    - thymine.
    - uracil.
  - The most common variation in a gene is the SNP (“snip”) which refers to:
    - single nucleotide polymorphism.
    - single new protein.
    - substituted nucleotide protein.
    - slow new polymorphism.
  - With a gene variant that is a “gain-of-function” form, drug metabolism will:
    - increase.
    - decrease.
    - remain the same.
  - Approximately what percent of drugs are metabolized by cytochrome P450 2D6 (CYP2D6)?
    - 5 percent
    - 10 percent
    - 20 percent
    - 75 percent
  - Codeine is a prodrug metabolized by what enzyme?
    - CYP1A2
    - CYP2C19
    - CYP3A4
    - CYP2D6
  - Individuals who are CYP2D6 poor metabolizers are at risk of morphine toxicity when taking codeine-containing products.
    - True
    - False
  - When a codeine-containing product is prescribed for a child following tonsillectomy, the therapeutic action is to:
    - use the normal pediatric dose.
    - use an alternative opioid or a non-opioid analgesic.
    - increase the dose to achieve analgesia.
    - decrease the dose to avoid toxicity.

**Completely fill in the lettered box corresponding to your answer.**

- |                    |                     |                     |
|--------------------|---------------------|---------------------|
| 1. [a] [b] [c] [d] | 6. [a] [b]          | 11. [a] [b] [c] [d] |
| 2. [a] [b] [c] [d] | 7. [a] [b] [c] [d]  | 12. [a] [b] [c]     |
| 3. [a] [b] [c]     | 8. [a] [b] [c] [d]  | 13. [a] [b] [c] [d] |
| 4. [a] [b] [c] [d] | 9. [a] [b] [c] [d]  | 14. [a] [b] [c] [d] |
| 5. [a] [b] [c] [d] | 10. [a] [b] [c] [d] | 15. [a] [b]         |

I am enclosing \$5 for this month's quiz made payable to: Ohio Pharmacists Association.

1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
  2. Did it meet each of its objectives?  yes  no  
If no, list any unmet \_\_\_\_\_
  3. Was the content balanced and without commercial bias?  
 yes  no
  4. Did the program meet your educational/practice needs?  
 yes  no
  5. How long did it take you to read this lesson and complete the quiz? \_\_\_\_\_
  6. Comments/future topics welcome.

Please print.

Program 0129-0000-13-012-H01-P  
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**Return quiz and payment (check or money order) to  
Correspondence Course, OPA,  
2674 Federated Blvd, Columbus, OH 43235-4990**

8. Following administration of carbamazepine, a patient with the *HLA-B\*15:02* gene variant and necrotic lesions on more than 30% of his body would be diagnosed with:

  - SJS.
  - MPE.
  - TEN.
  - erythema.

9. Genetic testing could be considered when initiating carbamazepine to avoid what potentially life-threatening condition?

  - Anaphylaxis
  - Heart attack
  - Stevens-Johnson syndrome
  - Stroke

10. What ethnicity has a higher frequency of the *HLA-B\*15:02* allele?

  - Asian
  - African American
  - Native American
  - Caucasian

11. Which guideline would you refer to for information about interpretation of genetic testing results?

  - Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7)
  - Infectious Disease Society of America (ISDA)
  - Adult Treatment Panel III (ATPIII)
  - Clinical Pharmacogenetics Implementation Consortium (CPIC)

12. Compared to their parent compound, how active are the hydroxy metabolites of tricyclic antidepressants?

  - Same activity
  - More active
  - Less active

13. When considering conversion of the prodrug clopidogrel to its active form, which gene has been mostly discussed?

  - a. *CYP2D6*
  - b. *CYP1E2*
  - c. *CYP3A4*
  - d. *CYP2C19*

14. Which of the following is the expected metabolic phenotype for a patient with a normal function allele and a loss-of-function allele in regards to *CYP2C19*?

- b. Poor metabolizer (PM)    d. Extensive metabolizer (EM)

To receive CE credit, your quiz must be received no later than December 15, 2016. A passing grade of 80% must be attained. CE credit for successfully completed quizzes will be uploaded to the CPE Monitor. CE statements of credit will not be mailed, but can be printed from the CPE Monitor website. Send inquiries to [opa@ohiopharmacists.org](mailto:opa@ohiopharmacists.org).

december 2013



**144<sup>TH</sup> Annual Meeting & Convention**  
**The Berkeley Oceanfront Hotel**  
**Asbury Park, NJ**  
**September 19-21, 2014**

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### PRELIMINARY PROGRAM SCHEDULE

#### **Friday, September 19th**

Registration Opens	12:00 PM-4:30 PM
Past Presidents Luncheon (invitation only)	1:00 PM-2:30 PM
Cross-Regional Roundtable Leadership Meetings	2:30 PM-3:30 PM
Committee Roundtable Meetings	3:30 PM-4:30 PM
Leadership Debrief (Regional, LO, Committee Chairs)	4:30 PM-5:00 PM
Welcome Reception & Special Award Presentation	6:00 PM-7:30 PM
Sponsored Evening Event-TBD	8:30 PM- 11:30 PM

#### **DINNER ON YOUR OWN**

#### **Saturday, September 20th**

Registration Open	7:30 AM-5:00 PM
Alumni Breakfast – Exhibits open	7:30 AM-9:00 AM
Student Volunteer and Shadow Briefing	8:00 AM-9:00 PM
Certificate Program Part 1*†	8:00 AM-12:00 PM
Student Track- Speed Networking	9:30 AM-10:30 PM
Continuing Education Program- Health Literacy	9:00 AM-10:00 AM
Professional Development- Dangerous Teen Trends ♦	9:00 AM-10:00 AM
Morning Break – Exhibits open	10:00 AM- 10:30 AM
Student Track- Pharmacy Student Self Care Competition	10:30 AM-12:00 PM
Continuing Education Program- Pharmacy Student Self Care Competition (NASPA)	10:30 AM-12:00 PM
Boxed Lunch – Exhibits open	12:00 PM-1:00 PM
Continuing Education Program- Disaster Management	1:00 PM-2:30 PM
Professional Development- Practice Spotlight Panel ♦	1:00 PM-2:30 PM
Benefits of Membership Presentation	2:30 PM-2:45 PM
Poster Session	2:45 PM-3:00 PM
Afternoon Break –Exhibits open	3:15 PM-3:30 PM
Continuing Education Program-New Drug Update	3:30 PM-5:00 PM
Student Track- Marketing Your Pharmacy Services	3:30 PM-5:00 PM
Professional Development- TBD♦	3:30 PM-5:00 PM
<b>Annual Meeting</b>	<b>5:00 PM-6:00 PM</b>
Evening Reception	6:00 PM-8:00 PM
Sponsored Evening Event-TBD	8:30 PM-11:30PM

#### **DINNER ON YOUR OWN**

\*Pre-registration required by 9/5, must attend BOTH Sat. & Sun. sessions

†Certificate Programs selections: Medication Therapy Management (MTM), Fundamentals of Pharmacy Counseling (NEW), or Compounding Essentials (NEW).

Registration is limited to one of the programs. See registration form for details

♦ Non-credit programs

#### **Sunday, September 21st**

Registration Open	7:30 AM-2:00 PM
Continental Breakfast- Exhibits open	7:30 AM-9:00 AM
Continuing Education Program- Medication Safety	8:00 AM-10:00 AM
Professional Development- Biosimilars Update♦	8:00 AM-10:00 AM
Certificate Program Part 2*†	8:00 AM-12:00 PM
Morning Break- Exhibits open	10:00 AM-10:30 AM
Continuing Education Program- New Anticoagulants	10:30 AM-12:00 PM
Professional Development- TBD ♦	10:30 AM-12:00 PM
<b>INSTALLATION LUNCHEON, AWARDS, AND KEYNOTE</b>	<b>12:00 PM-2:00 PM</b>
Continuing Education Program- Advocacy, Legislation, and Regulations (Law)	2:00 PM-3:30 PM

\*Pre-registration required by 9/5, must attend BOTH Sat. & Sun. sessions

† Certificate Programs selections: Medication Therapy Management (MTM), Fundamentals of Pharmacy Counseling (NEW), or Compounding Essentials (NEW).

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