

Pharmaci*s*ts Provide Care!

Spring 2020, Issue 12

Message from the President

Hello OCCP Members,

I look forward to the opportunity to serve as President of OCCP this year. Our organization has many exciting things to look forward to in the upcoming year.

In order to protect the health of our members, the executive committee has chosen to cancel the Spring OCCP meeting. This was a difficult choice to make but we know that it is the best for the wellness of our members and communities. We look forward to seeing you at the Fall 2020 meeting that will be held on October 9 at Tri-C Corporate College East. Our Steering and Planning committees have worked to identify meeting changes to best suit the needs of our membership. Look forward to updates on our Fall meeting format in the upcoming months.

Message from the President continued on page 2

OCCP Leadership

Sarah Petite, PharmD, BCPS President Liz Fredrickson, PharmD, BCPS President-Elect Steering Committee Chair Kelsey Rife, PharmD, BCACP Immediate Past President Katie Rivard, PharmD, BCPS, BCIDP, AAHIVP **Planning Committee Chair** Jessica Hoover, PharmD, BCPPS Secretary/Treasurer Andrea Pallotta, PharmD, BCPS, BCIDP Membership Committee Co-Chair Eve Hackett-Garr, PharmD, BCPS, BCIDP Membership Committee Co-Chair Karissa Kim, PharmD, BCPS Membership Committee Co-Chair SCCP chapter liaison Ellen Immler, PharmD, BCCCP Nominations Committee Chair Geralyn Water, PharmD, BCPS Advocacy Committee Co-Chair Katelyn Simmons, PharmD, BCACP Advocacy Committee Co-Chair Julia Kuroski, PharmD, BCCCP **Communications Committee Co-Chair** Sandra Axtell, PharmD, BCPS Newsletter Editor **Communications Committee Co-Chair** Keith Posendek, PharmD, BCPS, BCGP Newsletter Editor **Communications Committee Co-Chair**

Fall Meeting

Date: October 9, 2020

Location: Tri-C Corporate College East

Updates to Fall 2020 Meeting Include:

- Resident Track (e.g., wellness, project development, etc.)
 - Preceptor Track (e.g., continuing education, panel discussion, networking time)

Message from the President continued

President Message continued from page 1

Our Fall 2019 meeting was very successful! We were pleased with the venue change to Tri-C and the engagement from our members at this meeting. We have changed the focus from competitive judging of resident presentations and look forward to your continued feedback on these changes. We appreciate your feedback and are continuing to work to develop our organization to meet your needs.

Please visit our updated OCCP website if you have not had the opportunity to do so. The Communications committee did an excellent job updating the website to a more user-friendly format. While you are there, please remember to renew your membership dues. Thank you to the committee chairs and members for their continued hard work. If you are interested in joining a committee, you can volunteer on the Committee Membership page of our website's members only content.

Sarah Petite



Planning Committee Update

The 2019 Fall Meeting was very successful! The meeting was held for the first time at Tri-C Corporate College East. Highlights included a Medication Safety CE presentation by Dr. Susanna Petiya, PharmD, as well as variety of outstanding resident research presentations. We would like to thank members of the Planning Committee for all of their hard work in making the meeting a success.

Thank you,

Katie Rivard

Membership Committee Update

We are excited to announce the update to the membership renewal process. Membership now occurs on a rolling year basis, and not annually in January. This gives our members the flexibility to renew 12 months after paying the current year's dues. Please watch for an email on the first of the month that your membership will expire. When you renew, please consider joining a committee with OCCP. This is a great way to give back!

As we complete another academic year, we are always looking for OCCP members who are interested in giving back to our student SCCP chapters. In the past, members have presented at SCCP meeting on topics in their clinical practice area and summarized their current roles. It is a way to share your experiences and career path with our future Ohio pharmacists.

If you are interested in getting involved with the SCCP chapters,

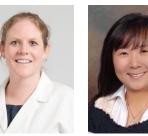
please reach out to one of the membership committee chairs.

Thank you,

Eve Hackett-Garr: <u>HACKETE@ccf.org</u>

Karissa Kim: kimky@ucmail.uc.edu

Andrea Pallotta: pallota@ccf.org





Advocacy Committee Update

In-person meetings and other gatherings have been cancelled, but pharmacy groups have continued to advocate for expanding pharmacists' role, this time with a new focus to provide high quality clinical care to patients in the setting of the novel coronavirus (COVID-19) pandemic. National pharmacy organizations, including ACCP, have come together with four recommendations for immediate adoption: (1) authorize test-treatimmunize, (2) ease operational barriers to address workforce and workflow issues, (3) address shortages and continuity of care, and (4) reimburse for services and remove barriers. More information available <u>here</u>.

The global COVID-19 pandemic has not halted pharmacy advocacy, but rather has served as a catalyst for greater traction on overcoming obstacles to expansion of the pharmacist's ability to deliver patient care.

Amidst the chaos of the global pandemic, pharmacy advocacy efforts have not halted, nor has the OCCP Advocacy Committee. At a regional, state, and federal level, the pandemic has served as a catalyst for greater traction on overcoming obstacles to expansion of the pharmacist's ability to deliver patient care.

The role of pharmacists in this national emergency has grown, and by September, there will be many examples of pharmacist services that should be made permanent or expanded as a result of pandemic. Also, we'll have many stories from around Ohio of how pharmacists stepped up with innovative services during this time of need. The forum will be an opportunity for those to be shared broadly with other pharmacists around the state.

As you'll recall, the Ohio Pharmacy Advocacy Forum will be this fall on September 25, 2020 at Ohio Northern University Raabe College of Pharmacy. Please save the date! The forum focus was originally decided to be drug pricing. However, with the COVID-19 pandemic and all the opportunities for pharmacists to play a major role in this national health emergency, the topic has been changed to COVID-19 and the Pharmacist.

We have been collaborating with our colleagues at Ohio Colleges of Pharmacy, the Ohio Pharmacists Association, and the Ohio Society of Health-System Pharmacists. This topic may also draw a broader group of legislators to the conference to discuss COVID-19 action and preparation for the future. The Ohio Pharmacy Advocacy Forum will be an excellent opportunity to learn more about this topic, to share your initiatives, and what YOU can do to help to make further strides in establishing pharmacist services as permanent post-pandemic. Please join us on September 25th, and contact an OCCP Advocacy Committee Chair if you'd like to be involved in the planning or events of the day. Thank you!

Brief Advocacy Updates:

In February, H.B. 341 passed the Ohio House of Representatives. This bill expands pharmacists' ability to administer any drug used for treatment of drug addiction or alcohol dependence, beyond just opioid antagonists.

Pharmacist Provider Status: Despite the passing of SB 265 in April 2019, granting provider status for Ohio pharmacists, Medicaid has not been able to continue with their efforts to roll out credentialing and providing essential Provider IDs that are necessary to put provider status into effect.

National Stage: Rutledge v Pharmaceutical Care Management Association (PCMA) is a Supreme Court case that seeks to support states' rights to pursue strategies to reduce drug costs and regulate PBMs. This issue originated in Arkansas, and is supported by Ohio Pharmacists Association.

HEROES of 2020 Act (H.R. 6433): To be negotiated into potential 4th COVID-19 legislative package by Congress. Provides a tax holiday for health professionals and first responders who continue to serve during the COVID-19 pandemic (up to \$50,000 of gross pay).

Pharmacists were NOT initially included as "first responders, but physicians, nurses, physician assistants, nurse practitioners, hospital and medical facility support staff, emergency medical technicians, paramedics, firefighters, corrections officers, and law enforcement officers" were recognized.

APhA's Governmental Affairs team spoke up for pharmacists and pharmacy technicians, who are now included on the bill!

COVID-19 Testing Approved for your Local Community Pharmacist: On 4/1/20, the Buckeye Institute drafted a proposal to leverage pharmacies as a part of the expansion of COVID-19 testing sites citing that "Pharmacists are trusted healthcare professionals with established relationships with their patients," and the "Vast majority of Americans live close to a retail or independent pharmacy."

Advocacy Committee Update continued on page 4

contact Keith Posendek

an article via our website (occpweb.org). We are looking for a clinical pearl and a new drug update for the fall newsletter. Requirements include 500 words maximum, clinically relevant topic, and at least one

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Advocacy Committee Update continued from page 3

On 4/8/20, the Department of Health and Human Services authorized licensed pharmacists to order and administer COVID-19 tests under Public Readiness and Emergency Preparedness (PREP) Act declaring a national emergency.

As we adjust to how COVID-19 has impacted our daily practices, from inpatient rounds to telework to virtual outpatient care, we can take a moment to think about how these adaptations in crisis may become our "new normal." OCCP has joined the Get the Medications Right (GTMRx) Institute as a Signing Member alongside other prominent pharmacy organizations like ASHP and ACCP. Communication briefs highlight the vision of GTMRx to leverage pharmacists and advance patient care with innovation! Please take a moment to check it out! Details at https:// gtmr.org/.

Finally, we want to say a huge THANK YOU to our Ohio Board of

Pharmacy for their readiness and prompt response to addressing a multitude of pharmacy issues during these difficult times.

Stay safe and healthy, and we will continue to provide advocacy updates as they arise!

Thank you,

Katie McMillan and Geralyn Waters



Communications Committee Update

Last fall, we released our updated OCCP website. For active members, to log into your account on the new website there are instructions on the home page. Once you log-in you will be able to update your account with your personal information. One of the features of the new website is the membership directory which allows you to connect with members in your area, or with members of your same clinical interests. The directory is available at: https://www.occpweb.org/membership-directory#! directory.

If you have any questions regarding your account or the website in general, please contact Julia Kuroski (kuroskj@ccf.org) or through the website at https://www.occpweb.org/contact.

Thank you to all the individuals that submitted articles for the spring newsletter. Thank you to Jessica Traeger, Kelsey Rife, and Sarah Petite for reviewing the spring newsletter article submissions.

If you are interested in writing an article or helping to review articles for future OCCP newsletters, please

(kposendek@westernreservehospital.org), or submit

author is an OCCP member.

The communications committee has resident and preceptor spotlights featuring one resident and one preceptor a quarter on the OCCP Facebook/Instagram page and newsletter. If you would like to nominate a resident or preceptor for this feature, submission information is available on the OCCP Facebook page or website.

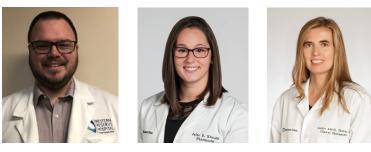
Be sure to follow us on social media to stay up to date with all **OCCP** activities!

Facebook: Ohio College of Clinical Pharmacy

Instagram: OCCP

Twitter: @OCCP clinical

Julia Kuroski, Sandra Axtell, and Keith Posendek







Nominations Committee Update

Due to COVID-19 and the cancelation of the spring meeting, the spring awards (BPS and pharmacist of the year) have been moved to fall 2020. The new application deadline is currently TBD.

Thank you,

Ellen Immler



Steering Committee Update

The Steering Committee has developed a proposal to create a Resident Advisory Committee. Residents who are selected for this committee would be responsible for assisting with developing resident- and student-focused programming for OCCP meetings, other resident- and student-focused initiatives, and potentially additional charges set forth by the OCCP Executive Committee. Our hope is to increase resident involvement within OCCP and to retain leaders for the organization upon their graduation. We hope to hold a future discussion with RPDs regarding this proposal.

Thank you,

Liz Fredrickson



Student Chapter Update University of Findlay

UF-SCCP planned a spring professional development event, where we organized a diabetes event to be held during a food pantry in the Findlay community. We had planned to do medication reconciliation, blood pressure screening, glucose readings, and A1c screenings as well. Unfortunately, this event had to be canceled due to the recent COVID-19 circumstances.

We are planning on organizing another event for a specialized pharmacist (transplant, ID) to talk with our classmates over

Zoom sometime during the remainder of the semester. Last semester we held an Sudden Cardiac Awareness Event where we made a poster and handed out pamphlets to students to educate them on this topic. We are currently trying to navigate how we are going to finish out the semester one day at a time and planning our nominations and clinical research teams for next semester!

Student Chapter Update University of Cincinnati

One of the events that we had was our pre-pharmacy mentoring meeting where we met with the pre-pharmacy student society from the UC Blue Ash campus. We were able to go over many topics that will help the students prepare to become a great candidate for applying to pharmacy school. This was not only a one-time event, but a career-long relationship builder.

One of the events that we had was our pre-pharmacy mentoring UC SCCP also got to color pages that will be sent to nursing meeting where we met with the pre-pharmacy student society homes and veterans, or anyone else in need of a smile.

Student Chapter Update Northeast Ohio Medical University

All of our events for the semester have been cancelled. Our local chapter's initial selection for the ACCP Clinical Research Challenge has been postponed to September. We're in the process of nominations for elections. After elections, we will hold our transition leadership meeting to hand-off duties to the new board.

Student Chapter Update University of Toledo

'S GOLDEN TICKET

The University of Toledo College of Pharmacy and Pharmaceutical Sciences (UTCPPS) SCCP chapter had a fun and exciting fall 2019 semester. In August, SCCP joined other UTCPPS pharmacy

organizations in welcoming the incoming class of student pharmacists to the professional division of pharmacy school.

Our 2019-2020 executive board [pictured below (L-R): Ryan Strausbaugh (President-Elect), Katherine Matousek (Secretary),

Megan Galle (Programming Coordinator), Brittany Curran (President), Emily Gonzalez (Historian); not pictured: Kaun Sturgill (Treasurer), Dr. Julie A. Murphy (Chapter Advisor)] hosted a table at the P1 Orientation Cook-Out to introduce the new class



to our SCCP chapter, explain the purpose of our organization, play medication hangman, and distribute candy bars each with a Golden Ticket that advertised our major events for the semester. Welcome week wrapped up with our Blaze Pizza fundraiser and the

first general meeting of the school year.

In September, we successfully hosted our 6th Annual Trivia Night, SCCP's biggest philanthropic event of the year. The turn-out was great, with 8 teams competing in ten rounds of general trivia questions. We were able to present a check for \$1,600 to support the Community Care Clinic - a



multidisciplinary student-driven free clinic that provides healthcare to the uninsured and underinsured citizens in Northwest Ohio.

Following Trivia Night, the SCCP chapter hosted a Residency Panel. The panel of PGY1 and PGY2 residents of various programs answered questions and provided advice to student pharmacists interested in pursuing residencies.

In celebration of our Founder's Day (October 4, 2013), we wanted to show our thanks to the UTCPPS students and fellow SCCP members for their continued support of the organization. We made dozens of individual cookie and M&M-filled bags to distribute in-between classes.





Thanks to the generous contributions of students, faculty, and staff, SCCP was able to donate 80 toys, books and games to the Hope for the Holidays campaign to support families in our community during the holiday season. All collected toys were given to local

families

through the Salvation Army and U.S Marine Corps Reserves (Toys for Tots) programs.

In February, we once again hosted our "Are You Smarter than a P1" event, a friendly competition between the P1, P2

and P3 classes that tests their knowledge on material taught during the first professional year. Not only were the P3 students victorious, but money was raised for the University of Toledo Medical Mission Trips.

The SCCP chapter of UTCPPS is excited to announce that our team for the ACCP Clinical Research Challenge has moved on to round 3 of the competition. The team (standing: Ryan Strausbaugh (Captain), Austin Verhoff; sitting: Elise Illius (alternate), Bianka Ahmetspahic)



University of Toledo Update continued on page 7



University of Toledo Update continued from page 6 are working on a full research proposal to compete in this final portion of the competition.

The rest of our spring semester will bring new challenges as the UTCPPS transitions to an all online class format. We will be holding our elections remotely. We are looking to reschedule most of our other events for next fall.



Student Chapter Update Cedarville University

In the fall our chapter had a lot going on. We have done many journal clubs encompassing topics such as important cardio landmark trials as well as how pharmacists can impact the outcomes for patients on antipsychotics. Our CNS PRN began with a meeting where we heard from a behavioral health specialty pharmacist and what it is like to work in psychiatric care. In February we had a meeting about what fellowship opportunities look like for pharmacists, what kinds of practice they apply to, and how they differ from residencies. Most notably our school's research competition team taking third in the nation! Due to COVID-19, the remainder of our spring plans have been changed

a little bit. We intend to do online meetings including one on what managed care looks like. Our field trips to Dayton Children's hospital and Nationwide Childrens' Behavioral Health Center have been canceled as well as the event hosting local grade school students in our practice lab and our Autism fundraiser 5K in order to prevent the spread of illness. We hope to reschedule these events next year as these are things that are important to us.



Clinical Pearl

Beta-Blocker use in Patients with Severe CAD but No History of a Cardiac Event

Benjamin Newell, PharmD, PGY-1 Resident; and Sandra Axtell, PharmD, BCPS Cleveland Clinic Hillcrest Hospital

Ischemic heart disease (IHD), also referred to as coronary heart disease, is characterized by an inadequate supply of blood to the myocardium due to obstruction of the coronary arteries mainly from atherosclerosis. Patients with IHD are referred to as stable (SIHD) when symptoms are reproducible primarily with exertion and are not progressing in severity.¹ Treatment with betablockers has been the standard of care for the past 40 years for patients with coronary artery disease (CAD) and prior myocardial infarction (MI).^{2,3} The evidence for the use of beta-blockers is derived from post-MI studies, but has been extrapolated to all patients with CAD with limited justification. The long-term efficacy of these agents is not well known since recommendations are based on studies with a maximum of 3 years of follow-up.⁴ Beneficial therapeutic effects of beta-blockade in patients with stable angina pectoris are mediated by a reduction in myocardial oxygen demand through heart rate, contractility, and left ventricular wall stress. These proposed effects have been considered to be the rationale for the use of beta-blockers in SIHD patients without a MI.¹⁻⁴ The 2012 expert panel for the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) guidelines in management of SIHD clas-

sifies cardioselective beta-blockers as a Class IIb, evidence C, in chronic therapy for patients with coronary or other vascular disease.² Common agents and dosing include metoprolol tartrate and atenolol titrated to a heart rate of 50-60 beats per minute.^{1,2}

The investigators of the 2012 international REACH registry compared the effect of beta-blockers to no beta-blockers in patient cohorts of CAD with prior MI, CAD without a prior MI, and those with only risk factors.⁴ This was an international, prospective, observational registry. CAD was defined as a history of percutaneous coronary intervention (PCI), coronary artery bypass graft surgery, or ischemia with or without a known history of MI. Risk factors were defined as at least three atherothrombotic risk factors such as elevated cholesterol, high blood pressure, smoking and diabetes. The analysis did not record data on type of betablocker and their rational was because there is no guideline recommendation on beta-blocker therapy except for reduced ejection heart failure. The REACH investigators also cited The Carvedilol Acute Myocardial Infarction Study (CAMIS) which showed no difference in cardiovascular composite when comparing carvedilol and atenolol with preserved ejection fraction as to why

Cohort (n=44,708)	Prior MI (n=14,043)	Documented CAD without MI (n=12,012)	CAD risk Factors (n=18,653) 3954/4854 (81%)	
BB use Propensity match	3379/9451 (36%)	3599/6864 (52%)		
Matched cohort no BB use	3379/4592 (74%)	3599/5148 (70%)	3952/13799 (29%)	
rimary Outcome Event rates BB vs no BB	489 (16.93%) vs. 532 (18.6%) HR 0.9 P=0.14	391 (12.9%) vs 405 (13.55%) HR 0.92 P=0.31	467 (14.22%) vs 403 (12.11%) HR 1.18 P=0.02	
Cardiovascular Death BB vs no BB	9.68% vs 10.27% P=0.31	5.9% vs 6.9% P=0.32	6.41% vs 6.4% P=0.66	
Nonfatal Stroke 4.44% vs 5.21% P=0.28 BB vs no BB		4.84% vs 4.79% 6.55% vs 5.12% P=0.06 P=0.39		
MI 5.5% vs 5.51% BB vs no BB P=0.42		3.79% vs 2.98% 2.82% vs 2% P=0.08 P=0.16		
Secondary Outcome BB use vs no BB use 30.96% vs 33.12%		30.5% vs 27.8% P=0.01	22% vs 20% P=0.04	
Hospitalization	23.1% vs 24.1%	24.1% vs 21.4%	14.62% vs 13.74%	
BB vs no BB	P=0.30	P=0.01	P=0.26	

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Clinical Pearl

Beta-Blocker use in Patients with Severe CAD but No History of a Cardiac Event

Benjamin Newell, PharmD, PGY-1 Resident; and Sandra Axtell, PharmD, BCPS Cleveland Clinic Hillcrest Hospital

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they did not track beta-blockers.⁵ The primary outcome was a composite of cardiovascular death, nonfatal MI, or nonfatal stroke. The secondary outcome was the primary outcome plus hospitalization for atherothrombotic events or a revascularization procedure. Based on results seen in Table 1, there was no added benefit or harm of beta-blocker use in patients with CAD or risk factors for CAD without prior MI.⁴

Another study analyzed data in the National Cardiovascular Data Registry for patients on beta-blocker therapy with CAD, defined as stable angina undergoing elective percutaneous coronary interventions (PCI), without prior MI (n=539,521) and those who were not taking beta-blockers (n=215,694).⁶ There was no difference in adjusted mortality rate (14.0% vs. 13.3%; adjusted HR: 1.00; 95% CI: 0.96 to 1.03; p=0.84), MI (4.2% vs. 3.9%; adjusted HR: 1.00; 95% CI: 0.93 to 1.07; p=0.92), stroke (2.3% vs. 2.0%; adjusted HR: 1.08; 95% CI: 0.98 to 1.18; p=0.14) or revascularization (18.2% vs. 17.8%; adjusted HR: 0.97; 95% CI: 0.94 to 1.01; p=0.10) with beta-blocker prescription. However, discharge on beta-blockers was associated with more heart failure readmissions at 3-year follow-up (8.0% vs. 6.1%; adjusted HR: 1.18; 95% CI: 1.12 to 1.25; p < 0.001).⁶ Beta-blocker use at discharge was not associated with any reduction in cardiovascular morbidity or mortality at 30-day and at 3-year follow-up.⁶

To date, there has not been a randomized, prospective, large trial to assess effects of beta-blockers on survival in patients with CAD without prior MI. The decision of whether to start a patient on a beta-blocker with CAD without history of a MI is difficult but key factors to consider are the patient's comorbidities and degree of symptoms such as exercise tolerance and breathing difficulties. If the decision is made to start a beta-blocker, a cardioselective beta-blocker should be started and is supported by the 2012 ACCF/AHA guidelines for management of SIHD.²

References:

- Kannam JP, Gersh B. Beta blockers in the management of stable ischemic heart disease. UpToDate. [Updated April 9, 2019; Accessed July 1, 2019].
- 2. Fihn SD, Gardin JM, Abrms J, Berra K, Blankenship JC, Dallas

AP. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease. Circulation. 2012;126:e354-e471.

- Beta-Blocker Heart Attack Trial Research Group. A randomized trial of propranolol in patients with acute myocardial infarction: II. Morbidity results. JAMA. 1983;250:2814–2819
- Bangalore S, Steg PG, Deedwania P, Crowley K, Eagle KA, Goto S. β-Blocker Use and Clinical Outcomes in Stable Outpatients With and Without Coronary Artery Disease. JAMA. 2012;308:1340-9.
- Jonsson G, Abdelnoor M, Muller C, Kjeldsen SE, Os I, Westheim A. A comparison of the two beta-blockers carvedilol and atenolol on left ventricular ejection fraction and clinical endpoints after myocardial infarction: a single-center, randomized study of 232 patients. Cardiology. 2005;103(3):148-155.
- Motivala AA, Parikh V, Roe M, Dai D, Abbott JD, Prasad A. Predictors, Trends, and Outcomes (Among Older Patients ≥65 Years of Age) Associated With Beta-Blocker Use in Patients With Stable Angina Undergoing Elective Percutaneous Coronary Intervention. J Am Coll Cardiol Intv. 2016;9:1639-48

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New Drug Update

Istradefylline: New Treatment Option for Off-Episodes in Parkinson's Disease

Anthony Wasielewski, PharmD Candidate, Northeast Ohio Medical University; Cindy King, PharmD, BCACP, CACP, MetroHealth System and Northeast Ohio Medical University

Background:

Parkinson's Disease (PD) is associated with a decrease in dopamine, causing motor disorders in patients. Currently, the mainstay of treatment is carbidopa/levodopa to replace the endogenous dopamine in the central nervous system (CNS). Often as patients progress, they experience "off" episodes as the amount of dopamine in the CNS decreases between doses. According to the 2018 Treatment of Motor Symptoms in PD Guidelines, dopamine agonists, catechol-o-methyltransferase (COMT) inhibitors, and monoamine oxidase-b (MAO-B) inhibitors, are considered efficacious in managing "off" episodes in patients taking carbidopa/levodopa for PD.¹

Istradefylline was FDA approved in August 2019 at a dose of 20 mg once daily (max dose is 40 mg/day) as an adjunctive treatment with carbidopa/levodopa in PD to decrease "off" episodes. The mechanism of action for istradefylline is unknown but has shown activity as an adenosine A_{2A} receptor antagonist in both *in vitro* and *in vivo* animal studies. No dose adjustments are recommended for renal impairment (defined as CrCl ≥15 mL/min) or mild hepatic impairment. In moderate hepatic impairment (Child-Pugh class B), a max dose of 20 mg daily is recommended, and data is lacking on use in CrCl <15 mL/min, hemodialysis, or severe hepatic impairment. The most common adverse reactions are dyskinesia, hallucinations/psychotic behavior, and impulse control/compulsive behaviors. ² Drug interactions include:²

- Strong CYP3A4 inhibitors max dose of 20 mg/day
- Strong CYP3A4 inducers avoid concomitant use
- Tobacco containing products recommend 40 mg/day if patient smokes > 20 cigarettes/day
- Use with CYP3A4 or P-glycoprotein substrates monitor for adverse reactions

Literature Review:

Four randomized, multicenter, double-blinded, 12-week, placebo-controlled trials have been completed evaluating the efficacy of istradefylline as adjunctive treatment with carbidopa/ levodopa. The primary efficacy endpoint for all studies was the change from baseline in the percentage of "off" time during daily awake hours or the total daily "off" time (Table 1). The sec-

ondary efficacy endpoint evaluated increase from baseline in "on" time without troublesome dyskinesia (Table 2). Overall, between these 4 studies, 1% of individuals on istradefylline 20 mg or 40 mg discontinued use due to dyskinesia compared to 0% in the placebo group.² All 4 studies showed a statistically significant decrease in the amount of hours with off symptoms compared to placebo. Clinically, these studies have shown a potential to decrease off symptoms in patients by 0.65-1.79 hours.

Table 1: Studies 1-4 Change from baseline in Awake "Off" Hours²

	Change from baseline in Awake "Off" Hours					
Study:	Placebo (hrs)	20 mg (hrs)	20 mg vs Placebo <i>(hrs)</i>	40 mg <i>(hrs)</i>	40 mg vs Placebo <i>(hrs)</i>	
Study 1 ³ (N=195)	-0.64	-	-	-1.79 (p=0.006)	-	
Study 2 ⁴ (N=225)	-0.9	-1.6 (p=0.0 3)	-	-	-	
Study 3 ⁵ (N=357)	-0.66	-1.31	-0.65 (p=0.013)	-1.58	-0.92 (p<0.001)	
Study 4 ⁶ (N=366)	-0.23	-0.99	-0.76 (p=0.003)	-0.96	-0.74 (p=0.003)	

Table 2: Studies 1-4 Change from baseline "On" time without troublesome dyskinesia²

Study:	"On" time without troublesome dyskinesia					
	Placebo (hrs)	20 mg <i>(hrs)</i>	20 mg vs Placebo <i>(hrs)</i>	40 mg <i>(hrs)</i>	40 mg vs Placebo <i>(hrs)</i>	
Study 1 ³ (N=195)	0.49	-	-	1.45 (p=0.026)	-	
Study 2 ⁴ (N=225)	0.70	1.3 (p=0. 14)	-	-	-	
Study 3 ^{2,5} (N=357)	-	-	0.57 (p=0.085)	-	0.65 (p=0.048)	
Study 4 ⁶ (N=366)	0.26	1.09	0.83 (p=0.003)	1.08	0.81 (p=0.004)	

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New Drug Update

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Conclusion:

Istradefylline is a novel adjunctive therapy to carbidopa/ levodopa in patients who need treatment of "off" episodes. The average wholesale price of istradefylline is \$60 per tablet.⁷ At this time, no data is available comparing istradefylline to dopamine agonists, COMT inhibitors, or MOA-B inhibitors, thus inferiority or superiority is unknown. Due to these factors, a trial of less costly mainstay options should be considered including dopamine agonists, COMT inhibitors, or MAO-B inhibitors. Istradefylline would be an appropriate alternative for those patients who have failed therapies listed above.

References:

- Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. Mov Disord. 2018;33(8):1248-1266.
- Nourianz[™] (istradefylline) [prescribing information] Bedminster, NJ: Kyowa Kirin, Inc.; October 2019.
- Lewitt PA, Guttman M, Tetrud JW, et al. Adenosine A2A receptor antagonist istradefylline (KW-6002) reduces "off" time in Parkinson's disease: a double-blind, randomized, multicenter clinical trial (6002-US-005). Ann Neurol. 2008;63(3):295-302.
- 4. Hauser RA, Shulman LM, Trugman JM, et al. Study of istradefylline in patients with Parkinson's disease on levodopa with motor fluctuations. Mov Disord. 2008;23(15):2177-85.
- Mizuno Y, Hasegawa K, Kondo T, Kuno S, Yamamoto M. Clinical efficacy of istradefylline (KW-6002) in Parkinson's disease: a randomized, controlled study. Mov Disord. 2010;25 (10):1437-43.
- Mizuno Y, Kondo T. Adenosine A2A receptor antagonist istradefylline reduces daily OFF time in Parkinson's disease. Mov Disord. 2013;28(8):1138-41.
- 7. Lexi-Comp Online. *Nourianz:* Drug Information. Hudson, Ohio: Lexi-Comp, Inc; October 2019.