The New Jersey
JOURNAL of Pharmacy

New Jersey Pharmacists Association
Spring 2018 • Volume XCII • Number 2

RETAIL • COMMUNITY • COMPOUNDING • HEALTH SYSTEM
DISASTER MANAGEMENT • CONSULTANT • INDUSTRY • ACADEMIA
PHARMACY TECHNICIANS

Peer Reviewed

New Jersey Pharmacists Association
148th Annual Meeting & Convention
November 9th through 11th, 2018

FRIDAY, NOVEMBER 9TH	
Registration Open	7:00 AM – 4:00 PM
Diabetes Certificate Training – Part 1	8:00 AM – 12:00 PM
MTM Certificate Training – Part 1	8:00 AM – 12:00 PM
CPR Red Cross Certification Training	8:00 AM – 12:00 PM
New and Revised Labeling for Commonly Prescribed Medications – L. Gooen	10:00 AM – 12:00 PM
LUNCH	12:00 PM – 1:30 PM
Cancer Survivorship & The Pharmacist – J. Timoney	1:45 PM – 3:45 PM
NJPhA Annual Meeting & Committee Presentations	3:45 PM – 5:00 PM
Welcome Reception	5:00 PM – 6:00 PM

SATURDAY, NOVEMBER 10TH	
Registration Open	7:00 AM – 4:00 PM
BREAKFAST in Exhibit Hall	7:30 AM – 9:00 AM
Diabetes Certificate Training – Part 2	8:00 AM – 12:00 PM
MTM Certificate Training – Part 2	8:00 AM – 12:00 PM
Immunization Refresher 2018 – A. Crochunis	9:00 AM – 11:00 AM
Keynote Presentation	11:00 AM – 11:30 AM
Poster Session	11:30 AM – 12:30 PM
LUNCH in Exhibit Hall	12:00 PM – 1:30 PM
Testing Your Medical APP-titude – N. Owens	1:30 PM – 3:00 PM
Legislative Hearing	3:00 PM – 4:30 PM
Student Pharmacist Self Care Championship	4:30 PM – 6:00 PM
+TONICRx Happy Hour	6:00 PM – 7:30 PM
Healthcare Providers Dinner* *Subject to Change	7:45 PM – 9:45 PM

Student Activities
10:00AM–6:00PM

- √ Orientation
- √ Legislative Hearing
- √ Communication Skills Training
- √ Student Championship
- √ Networking Reception

SUNDAY, NOVEMBER 11TH	
Registration Open	7:30 AM – 1:00 PM
BREAKFAST in Exhibit Hall	7:30 AM – 9:30 PM
Specialty Drugs – J. Colaizzi	9:30 AM – 11:00 AM
Check-Out Break	11:00 AM – 11:30 AM
Installation & Awards Luncheon	11:30 AM – 1:30 PM
Law Program – A.Cifaldi & S.Poondi	1:30 PM – 3:00 PM

*Schedule & Program Titles Subject to Change

As of April 20, 2018

The New Jersey Journal of Pharmacy (ISSN0028-5773 USPS #380-360) is published seasonally by the New Jersey Pharmacists Association
760 Alexander Road, PO Box 1
Princeton, NJ 08543-0001
609-275-4246 Fax 609-275-4066
www.njpharmacists.org

Periodicals Postage Paid at Princeton, NJ and additional mailing offices. Subscriptions paid for through allocation of membership dues. US Subscription **$50 per year;** Foreign Rate **$100 per year**.

POSTMASTER: Send address changes to The New Jersey Journal of Pharmacy, 760 Alexander Rd., PO Box 1, Princeton, NJ 08543-0001. 609-275-4246. www.njpharmacists.org

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Stay Connected with NJPhA

Mission Statement:

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

President's Letter

2018 has been an exciting year so far at NJPhA. In March, the professional affairs task force on the labeling of gluten in medication successfully introduced policy to the APhA House of Delegates. The task force, that included members Jane Bowen, Aakash Ghandi, Christina Zikos, Steve Zlotnick, Tatiana Sanchez, Ashley Job and Karishma Patel, also provided comment to the FDA on their proposed guidance to industry.

In addition, we are awaiting upcoming legislative hearing schedules, the next step in advancing the pharmacy student immunization bill.

The association has been gaining momentum in part through the variety in leadership among our trustees and officers. This is the time of year when we ask each member to search their hearts and ask, "Do I have something to give that can help advance the profession and bring my fellow pharmacists together? Should I submit my name and run to be the next officer to join the line as vice president? The commitment is for 4 years as a leader progresses through the leadership positions of "the line". The vice president heads the membership drive and learns about what it takes to keep the organization going. In the second year, the elected member advances to be president-elect and chairs the convention committee. At that convention they are sworn to the office of president for their third year of service. After completing a year as president, the next step is to serve as the chair of the board of trustees. NJPhA looks each year for someone who is an active member with leadership skills and devotion to the profession. As an officer, the successful candidate joins the board of trustees in protecting the association and the profession of pharmacy in our state. To all of those members who have been active and held positions of leadership in our organization I ask you- **Is it your time?**

Carmela Silvestri, PharmD, CCP

From The Editors' Desks...

Dear Colleagues,

Thank you for your continued support for the *New Jersey Journal of Pharmacy* – the official peer-reviewed journal of the New Jersey Pharmacists Association. The Journal Committee is excited to present new articles for your reading pleasure! Please keep your manuscripts and Spotlight articles coming!!! It is our hope that you enjoy the Spring edition of our journal.

Please consider becoming active in the development of the *New Jersey Journal of Pharmacy,* through either submission of an article, being the spotlight in pharmacy or becoming a peer-reviewer. If interested please reach out to me, Julie Kalabalik, Elise Barry, or one of the NJPhA officers. You may email ideas and submissions to marcella.r.brown@gmail.com or j.kalabalik@gmail.com. We can help you with a topic consideration for the journal.

I wanted to thank you and look forward to your submissions!

Marcella

Marcella R Brown, BS, MS, PharmD, MPH, CGP, BCACP
Julie Kalabalik, PharmD, BCPS, BCCCP
Co-editors of the *NJPhA Journal of Pharmacy*

Upcoming Journal Deadlines

Summer 2018 - July 15, 2018

Fall 2018 - October 12, 2018

Winter 2019 - December 21, 2018

Message from the Chair of the Board of Trustees

As Chair of the Board of Trustees for 2018 and immediate NJPhA Past President, I, along with our CEO and officers, want to consistently hear from our members throughout all of New Jersey. The BOT, among its many responsibilities, is to consider and act upon all matters of NJPhA business and ensure that all NJPhA regions remain active.

In case you are not aware, NJPhA has divided New Jersey into 6 regions, each with its own leadership and trustee representative to the BOT. All of the regions work hand in hand with the NJPhA office to provide CE programming, social events, and to assist with membership recruitment and retention. It is evident that now, more than ever, your input and participation is needed statewide.

A list of regional presidents and region trustee representatives and their e-mail is provided. We encourage you to contact your regional leaders. Tell them what's on your mind and even better, volunteer to assist them with their regions organization activity. NJPhA and your profession would be better for it.

Ronald J. Mannino, RPh

Region 1: Bergen
President: Ron Mannino ron@interchem.com
BOT Trustee: Salvatore Peritore SALPERITORE@hotmail.com

Region 2: Essex, Hudson, Morris, Passaic, Union, Sussex
President: Henry Gialanella hgialanella@gmail.com
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President: Adedolapo (Dolly) Ademodi-Gbogodo
drgbogodo@msn.com
BOT Trustee: Tony Qi, PharmD tonyqi33@gmail.com

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President & BOT Trustee: Ruth Marietta ramar040@optonline.net

Region 5: Atlantic, Cape May, Cumberland, Salem
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BOT Trustee: Mark Taylor mtaylor@curexa.com

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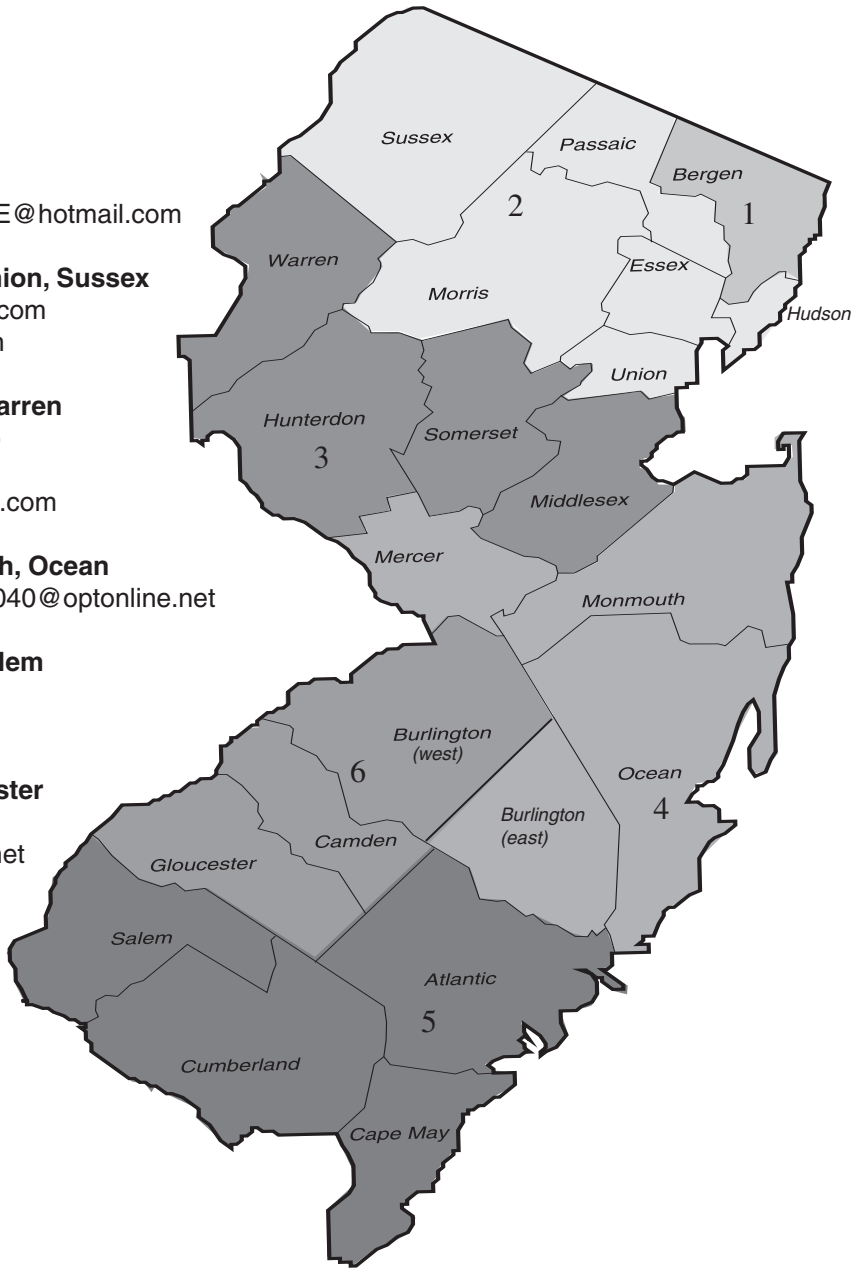
President: Azuka Obianwu aobianwu@aol.com
BOT Trustee: Richard Kress richrx1@comcast.net



Class Review of Cystic Fibrosis Transmembrane Regulator (CFTR) Modulators

Priya Narang, PharmD, MS; Christine Lam, PharmD, BCPS, CDE, BCACP, BCGP; Rebecca Griffith, MD

Introduction:
Cystic Fibrosis (CF) is an autosomal recessive disease characterized by abnormal airway secretion, chronic endobronchial infection, and progressive airway obstruction. While the disease affects multiple organs, 85% of CF mortality is a result of lung disease. Almost 1,000 new cases are diagnosed nationally each year and more than 80,000 people are affected worldwide. Cystic fibrosis arises due to the *CFTR* gene mutation that disrupts proper regulation of salt and water absorption. The CFTR modulators are a class of medications with multiple mechanisms that act synergistically to improve lung function. This review will incorporate pharmacology, efficacy, safety, and the current place in therapy of the three medications in this class.[1]

Pathogenesis of CF:
Cystic fibrosis is characterized by six different classes of CFTR channel protein mutations that affect abnormal chloride transport (Table 1).

Class I mutations, caused by mutations that either prematurely stop or interfere with CFTR channel protein production, result in a lack of CFTR protein production. Twenty-two percent of patients are diagnosed with a class I mutation, examples of the mutation include: W1282X, R553X, and G542X.

Class II mutations result in misfolded CFTR proteins, which prevents correct CFTR cellular placement. F508del is a mutation that is commonly expressed in this class, with 50% of patients being homozygous for the mutation and 90% carrying at least one copy of it. Overall, 88% of patients are diagnosed with a Class II mutation.

Class III mutations, known as the gatekeeper mutation are characterized by a substitution of amino acids, which disrupt the regulation of the CFTR channel. Consequently, there is a reduction or lack of the CFTR channel opening. G551D is the most common mutation seen in patients in this class. Approximately 6% of CF patients are classified with a class III mutation.

Patients with a class IV mutation are characterized with a molecular defect. For example, substitution of amino acids may result in changes to the protein structure that forms the pore of the channel. Ultimately, the misshaped CFTR pore restricts the movement of chloride ions through the channel. Examples of mutations in this class include R117H, R334W, and R347P. Roughly 6% of CF patients are classified with a class IV mutation.

Class V mutations are characterized by an insufficient amount of protein. It is hypothesized that mRNA processing is disrupted through alternative splicing. Consequently, there is a severe reduction in the amount of normal CFTR proteins that are synthesized. About 5% of patients are classified with a class V mutation.

Class VI mutations, classified in less than 1% of CF patients, result in functional, but unstable, CFTR proteins. The protein is quickly removed and degraded, which results in increased turnover of the CFTR channel.[2]

CFTR modulators
The class of CFTR modulators consists of three medications: KALYDECO (ivacaftor), ORKAMBI (lumacaftor/ivacaftor), and SYMDEKO (tezacaftor/ivacaftor). This new class of medications depends upon the CFTR mutation in each individual patient. Prior to initiation, all CF patients will undergo genotyping of their CFTR to evaluate the drug for which they are eligible.

Ivacaftor (KALYDECO)
Ivacaftor was approved by the Food and Drug Administration (FDA) in 2012 and targets the G551D mutation. This drug is approved in those 2 years or older with one of 23 specific mutations, such as E56K, G178R, and S549R.[3]

Mechanism of action
Ivacaftor acts as a potentiator, in turn increasing the opening time of the CFTR channel, ultimately resulting in higher ion flow. It increases the amount of time the CFTR channel remains open, augmenting chloride transport.[3]

Pharmacokinetics
This medication is given orally. Exposure in the CFTR modulators has been shown to increase approximately 2.5 to 4-fold when taken with high fatty food[3]. Plasma concentrations for ivacaftor peak at approximately four hours. The elimination half-life for ivacaftor following a single dose is approximately 12 hours. Ivacaftor is approximately 99% protein bound and about 88% of it is eliminated in the feces. Furthermore, the dose of ivacaftor must be adjusted when administered with CYP 3A4 strong inhibitors.[3]

Clinical trials
Ivacaftor was approved based on a clinical trial in 2011 which evaluated the efficacy of the medication. The study was a randomized, double-blind placebo-controlled trial that consisted of 161 patients. The primary endpoint evaluated the estimated mean change from baseline through week 24 in the percent of predicted forced expiratory volume in 1 second (FEV1). Results illustrated that the change from baseline through week 24 in percent of predicted FEV1 was greater by 10.6% in the ivacaftor group versus the placebo group. Another study evaluated the same conditions,

Table 1:

Class	I	II	III	IV	V	VI
Mechanism of Action (MOA)	Defective protein production	Defective processing of protein	Reduction or lack of CFTR channel opening	Molecular defect	Insufficient amount of protein	Increased turnover of CFTR channel
Mutations	W1282X, R553X, G542X	F508del	G551D	R117H, R334W, R347P	A445E	120del23, N287Y
Medications		lumacaftor/ivacaftor, tezacaftor /ivacaftor	Ivacaftor			
Frequency	22%	88%	6%	6%	5%	< 1%

however, the population was slightly different as participants were between 6 and 11 years of age and possessed the G551D mutation. The primary endpoint of this study also evaluated the absolute change from baseline through week 24 of predicted FEV1. Results illustrated that the mean absolute increase from baseline was 12.6% in the percent of predicted FEV1 in the ivacaftor group vs 0.1% in the placebo group. Also, the adjusted change in percent of predicted FEV1 from baseline through week 48 was 10% greater with ivacaftor versus placebo.[4]

Safety

The overall safety profile of ivacaftor was based on data from three placebo-controlled trials which were conducted in patients 6 years of age or older who either possessed the G551D mutation or tested homozygous for the F508del mutation. Two percent of patients prematurely discontinued the study drug compared to 5% for placebo-treated patients. Similarly, serious adverse events that occurred more frequently in the study group compared to placebo included abdominal pain, increased liver function tests (LFTs), and hypoglycemia. The most common adverse events observed included headache, upper respiratory tract infection, nasal congestion, nausea, and rash.[3]

Lumacaftor/ivacaftor (ORKAMBI)

Mechanism of action

Lumacaftor/ivacaftor was approved by the FDA in 2015 and targets the F508del mutation, which improves the conformational stability of the protein, resulting in increased processing and trafficking of the mature protein to the cell surface.[5]

Pharmacokinetics

In the presence of fatty foods compared with a fasting state, lumacaftor exposure is approximately two times higher, while ivacaftor exposure is approximately three times higher. After multiple doses, exposure generally increased proportionally to the dose. Plasma concentrations of lumacaftor/ivacaftor peaked at approximately four hours in the fed state. The elimination half-life of lumacaftor was about 26 hours. Lumacaftor is approximately 99% protein bound, and the majority of it is excreted unchanged in the feces. Minimal elimination of lumacaftor and its metabolites was shown in the urine. Furthermore, the dose of lumacaftor/ivacaftor must be adjusted when administered concomitantly with CYP 3A4 moderate and strong inhibitors.[5]

Clinical trials

Lumacaftor/ivacaftor was approved in 2015 after a trial assessed the effects of lumacaftor in combination with ivacaftor, in patients who were homozygous for the F508del mutation. The trial was a phase III, randomized, a double-blind placebo-controlled trial whose primary endpoint was the absolute change from baseline in percentage of predicted FEV1 at week 24. The mean baseline FEV1 was 60.5% and results showed a statistically significant difference in the mean absolute change in the percentage of predicted FEV1 by 4%. Similarly, a statistically significant difference was shown in the improvement of predicted FEV1 of 5% or higher in the lumacaftor-ivacaftor group versus placebo. Similar to ivacaftor, this trial also evaluated patients who were at least 12 years of age. Therefore, another trial was completed, which evaluated the efficacy of lumacaftor/ivacaftor in pediatric patients aged 6-11 years. This was an open-label phase III trial which evaluated lung function based on FEV1. The mean baseline FEV1 of patients in the study was 91.4%; however, results demonstrated an increase in FEV1 of 2.5% by week 24 in the active treatment group.

Safety

Safety studies for lumacaftor/ivacaftor were based on a population of 1,108 patients who were homozygous for the F508del mutation in the CFTR gene and who received at least one dose of the study drug in two double-blind placebo-controlled phase 3 trials. Five percent of lumacaftor/ivacaftor patients prematurely discontinued the study drug compared to 2% of patients who received the placebo. Serious adverse events that occurred more frequently in the active treatment group included pneumonia, hemoptysis, cough, and increased LFTs. Similarly, safety studies were also conducted in pediatric patients aged 6-11 years who were homozygous for the F508del mutation. This was a 24-week, open-label, phase III, multicenter trial. Adverse reactions that occurred in at least five percent of lumacaftor/ivacaftor patients included productive cough, nasal congestion, headache, upper abdominal pain, and increased sputum.

These events occurred more frequently in the active treatment group compared to placebo. Other types of reactions that occurred in the lumacaftor/ivacaftor group included menstrual abnormalities and hypertension. Menstrual abnormalities were found to be more common in the subset of patients using hormonal contraceptives compared to patients who were not. Similarly, adverse reactions related to increases in blood pressure were reported in about 1% of patients in the lumacaftor/ivacaftor group versus no patients in the placebo group. Hypertension in this population was defined as a blood pressure >140/90 mmHg. Therefore, blood pressure in these patients should be routinely monitored.[5]

Tezacaftor/ivacaftor (SYMDEKO)

Mechanism of Action:

Tezacaftor/ivacaftor, approved by the FDA in February 2018, targets the F508del mutation. Also, tezacaftor increases the amount of mature CFTR protein that is delivered to the cell surface, while ivacaftor acts to potentiate CFTR proteins.[7]

Pharmacokinetics:

The exposure of tezacaftor/ivacaftor has also been shown to increase with fat-containing foods. After a single dose, ivacaftor exposure is approximately three times higher compared to a fasting state. Tezacaftor and ivacaftor are both approximately 99% protein bound. Following oral administration of tezacaftor, about 72% of the dose is excreted in the feces, the majority of which is unchanged. Less than 1% of the dose was excreted in the urine as unchanged tezacaftor, illustrating that the major pathway of elimination for tezacaftor is not through renal excretion. Also, the dose of tezacaftor/ivacaftor must be adjusted when administered concomitantly with CYP 3A4 moderate and strong inhibitors.[7]

Clinical trials

In a trial which evaluated tezacaftor/ivacaftor in patients that were homozygous for the F508del mutation, the primary outcome of the study was the absolute change in the percentage of predicted FEV1 from baseline through week 24. The mean baseline FEV1 was shown to be variable and ranged from 44.9% to 74.3%. Results demonstrated that there was a statistically significant greater absolute change by 4% from baseline in percentage of predicted FEV1 versus placebo. Similarly, the mean absolute change from baseline through week 24 improved by 3.4% in the tezacaftor/ivacaftor group versus 0.6% in the placebo group.[8]

Safety

The overall safety profile of tezacaftor/ivacaftor was based on data from three double-blind, placebo-controlled, phase III trials. 3.1% of placebo patients discontinued the trial prematurely due to adverse events versus 2.8% of tezacaftor/ivacaftor patients. 0.6% of tezacaftor/ivacaftor experienced distal intestinal obstruction syndrome compared to no patients in the placebo group. The most common side effects (> 10%) observed in both groups included: cough, headache, pyrexia, nasopharyngitis, and increased sputum production. These events were more frequently noted in the placebo group compared to the treatment group. There was one death reported in the active treatment group due to respiratory failure and influenza in a patient who had discontinued tezacaftor/ivacaftor seven weeks prior. No deaths were reported in the placebo group.[7]

Place in Therapy

The CFTR modulators are considered a first-line therapy for patients with the specific mutations that the medications target. Deciding which modulator to initiate should be based on the patient's specific gene mutation. Patients with the G551D mutation should be initiated on ivacaftor. Those with the F508del mutation are not appropriate for ivacaftor. Therefore, lumacaftor/ivacaftor or tezacaftor/ivacaftor are suitable choices for those patients.

However, if the patient's baseline FEV1 is 40% or less, use of lumacaftor/ivacaftor is recommended with caution. A retrospective cohort study was conducted, which analyzed the clinical experience of this medication in CF patients.[9] Results showed that 19 patients had an FEV1 ≤ 40%. Consequently, a higher percentage of adverse events was observed in this population (57.9%) versus those who had a higher FEV1 at baseline. Similarly, 31.6% of patients with an FEV1 ≤ 40% did have to discontinue treatment. Ultimately, this is a factor that should be taken into account prior to starting treatment.

Key counseling points

Each of these medications should be taken with fat-containing food due to greater absorption (e.g., eggs, butter, peanut butter, pizza, and whole-milk dairy products). If a dose is missed within 6 hours of the time usually taken, patients should take the prescribed dose with fat-containing food as soon as possible. If more than six hours have passed, the patient should skip that dose and resume their regimen as normal.[3,5,7]

Monitoring parameters

With this class, LFTs should be drawn at baseline, every three months for the first year, and then annually. If ALT/AST reach five times the upper limit of normal, the medication should be temporarily discontinued until levels are back to normal. Other mild side effects that patients may experience include gastrointestinal intolerance, headache, or upper respiratory tract infection. For patients treated with lumacaftor/ivacaftor, blood pressure should be regularly monitored while on therapy, since hypertension has been known to occur. Similarly, menstrual abnormalities are another concern to take into consideration while patients are on lumacaftor/ivacaftor. This class has not been studied in severe renal impairment, therefore, caution is advised. Also, dose adjustments are required for moderate to severe hepatic impairment. Furthermore, because these medications do interact with moderate and strong 3A4 inhibitors, an interaction check should be conducted prior to starting therapy. [3,5,7]

Conclusion

While these medications have brought about a novel

approach to the treatment of CF, more research is in the pipeline. Trials currently underway are investigating the use of CF medications as a corrector as well as an amplifier. Ultimately, the discovery into the world of CF has only begun.

About the Authors:
Priya Narang, PharmD, MS
PGY-1 Pharmacy Practice Resident
Atlantic Health System
Email: pnarang87@gmail.com

Christine Lam, Pharm.D., BCPS, CDE, BCACP, BCGP
Clinical Assistant Professor of Pharmacy Practice
Fairleigh Dickinson University School of Pharmacy and Health Sciences
Email: Clam42@fdu.edu

Rebecca Griffith, MD
Associate Director of Adult Cystic Fibrosis Center
Department of Medicine
100 Madison Avenue
Morristown, NJ 07962
Email: rebeccas.giffith@atlantichealth.org

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The Transition of Care Pharmacist: Transitioning Barriers to Success

Sibyl Marie Cherian, PharmD, BCPS, BCGP; Julie Kalabalik, PharmD, BCPS, BCCCP; Malgorzata Slugocki, PharmD; Amulya Uppala, PharmD, BCPS

Background

Transitions of care (TOC) indicate the concept of shifting patients between and among health care practitioners, settings, and home as the patients' conditions and specific needs change.[1] The movement can occur within settings (e.g., primary care to specialty care, or intensive care unit to a general medicine floor), between settings (e.g., hospital to sub-acute care; ambulatory clinic to senior center), across health states (e.g., curative care to palliative care, or personal residence to assisted living), or between providers (e.g., generalist to a specialist practitioner, or acute care provider to palliative care specialist).[2]

TOC involves a set of interventions aimed to ensure coordination and continuity of care. Ideally, they should be based on comprehensive care plans and the availability of well-trained practitioners who have current information about the patient's treatment goals, preferences, and health or clinical status. They also include logistical arrangements and education of patients and families, as well as coordination among health professionals involved in the transition.[2]

The Role of Pharmacists in Transitions of Care

The role of pharmacists in TOC is crucial and diversified. As medication experts and members of the healthcare team, pharmacists hold a unique position in enhancing medication management and reducing avoidable hospital readmissions for patients who are being transitioned from one practice setting to another. The National Transitions of Care Coalition recommends strategies to improve TOC, including assessing safe use of medication management by the patient, ensuring a formal process for safe care transitions, engaging patients in decision-making through education, and facilitating follow-up care.[3]

Published literature supports the impact of pharmacists in TOC. Services provided by TOC pharmacists can include collecting medication history and reconciliation, inpatient pharmacotherapy review, discharge medication counseling, discharge medication dispensing at bedside (meds-to-beds programs), coordination of patient-specific prescription coverage barriers, post-discharge clinic involvement, follow-up phone calls, home visits, and medication therapy management (MTM).[4] In addition, pharmacists screen for adherence concerns, drug-related problems, round with multidisciplinary teams, and communicate with other healthcare professionals involved in the patient's medical care.[5] A systematic review and meta-analysis by Rodrigues and colleagues showed a 32% reduction in odds of readmission (OR 0.68; 95% CI 0.61-0.75) for pharmacy-supported TOC interventions when compared to usual care, and interventions with patient-centered follow-up decreased 30-day readmission compared to those without follow-up (OR= 0.70; CI 0.63-0.78).[6] In one study, 30-day hospital readmission rates and emergency room (ER) visits were significantly less in patients who received a phone call from a pharmacist within 24 days post-discharge compared to patients whom the pharmacist could not contact ($p = <0.001$).[7] Cavanaugh and colleagues found a significant reduction in 30-day readmission rate in patients at moderate to high risk for readmission when seen by a pharmacist-coordinated multidisciplinary team compared to care by physicians only (14.3% vs 34.3%, $p = 0.010$). In addition, a multidisciplinary team which included a pharmacist addressed significantly more adherence issues (98.5% vs 86.8%, $p = 0.017$%), increased initiation of new medications for medical problems (60.9% vs 37.7%, $p = 0.010$), and increased resolution of polypharmacy issues (31.4% vs 15.7%, $p = 0.046$%).[8]

Barriers to Transitional Care Services

Despite the clear benefits to pharmacist involvement in TOC, there are several key barriers that must be identified and overcome in order to implement a well-coordinated TOC service.

Medication history and reconciliation

Although it is recognized that medication reconciliation prevents medication errors and decreases healthcare costs, the most obvious and often-cited barrier to medication reconciliation is lack of time.[9,10] In a recent evaluation of community pharmacists' perspectives on medication reconciliation, several pharmacists expressed difficultly in reaching inpatient prescribers and frustrations with the long turnaround time to achieve optimal results.[10] Furthermore, from an inpatient admission medication reconciliation perspective, time spent can range between 15-20 minutes per medication reconciliation[11–13] In addition, another challenge from the inpatient setting lies with contacting primary care providers, specialists, pharmacies, facilities and other points of information to complete an accurate medication reconciliation. Even with the most diligent medication history, it is still possible to miss important over the counter (OTC) or herbal supplements that only the patient or caregiver is able to disclose. This may require contacting family members or interviewing the patient several times during their hospital stay in order to get a complete medication history.

Some potential ways in which some of these barriers could be overcome is to create a systematic method in which medication reconciliation is performed. A medication reconciliation toolkit developed through Multi-Center Medication Rec-

onciliation Quality Improvement (MARQUIS)[14] can be used in order to train ancillary staff, such as pharmacy technicians, pharmacy residents and student pharmacists. In addition, healthcare systems can utilize database platforms, such as MedHx® through DrFirst®, in order to obtain insurance records of medications picked up from specific pharmacies. In some situations, if a patient is not alert and oriented to give medication information but may be taking controlled substances, a prescription monitoring program (PMP) can be useful to determine the pharmacy that the patient goes to in order to obtain the complete medication history. Along with PMP and database platforms, the creation of a universal or integrated electronic medical record (EMR) can save time and prevent communication barriers between various settings and providers. Despite all of these measures to save time, it is important to keep in mind that a patient or family interview is often still necessary in order to resolve discrepancies that often come to light when performing a medication history. Finally, completing an adequate medication history and reconciliation at admission can help the process of discharge medication reconciliation. This is because electronic medical records often use the admission medication reconciliation to begin the process of discharge medication reconciliation. Errors in this process can lead to increased and unnecessary utilization of resources to correct a problem that occurred in a different setting or with a different provider.

Discharge education and reconciliation

Although it is generally well-accepted that discharge education is a useful tool to improve TOC from the inpatient to outpatient setting, several studies have identified that significant challenges can exist when attempting to provide discharge education. One barrier highlighted is the inability to easily track patients during their inpatient stay to the point of discharge. In the study by Pherson and colleagues, service providers originally had to manually track their patients up until the point of discharge in order to schedule a home-visit post-discharge. In order to overcome this barrier, a daily report was created to alert service coordinators of discharge.[15] Another barrier is the lack of 24-hour pharmacy TOC services, thus leading to patients at discharge who may not be able to receive pharmacy TOC services.[16] The formation of a TOC team within a hospital setting may help to mitigate the problems that can arise. Ideally, the team should be multi-disciplinary in nature, as literature has suggested utilizing nurses, physician residents, pharmacy residents, student pharmacists and pharmacy technicians to provide coordinated TOC services.[8,17,18]

An accurate discharge medication reconciliation will serve as a list for the patient to bring to an outpatient provider or community pharmacy, which will then save time for those providers who perform outpatient medication reconciliation. When looking at the healthcare system as a whole, it is important to understand that the medication reconciliation process is a pivotal point of communication between settings and healthcare providers. Often times, inpatient TOC studies do not include information regarding collaboration with outpatient pharmacists and providers. To overcome this barrier, in addition to the usual TOC services, Farris and colleagues also sent a discharge care plan via fax to community pharmacists and physicians.[19]

Another important point to consider is the feasibility of the discharge process. According to Newman and colleagues, it may take a median of 57 minutes to complete the whole process of medication reconciliation, provider communication, and patient education.[20] Thus on any given day, one full-time equivalent pharmacist can only see an average of seven to eight patients. However, when coordinating discharge planning with outpatient providers as demonstrated by Farris and colleagues, this time spent can be as much as 210 minutes per patient.[19] To overcome this barrier, it is important for pharmacists to have accurate documentation of the time spent and interventions done in order to expand the services to more patients.

Post-discharge

Follow-up phone calls and home visits are potential ways to provide post-discharge TOC services. However, studies have cited that about 30% of patients are lost to follow-up.[15,16] Few studies discuss the time spent completing TOC services, but among the ones that do report the data, the time required for phone call follow-ups and clinic visits may be a potential barrier to provide post-discharge care.[15,21] Pharmacy post-discharge clinic visits can average about 45 minutes per patient and focus on identifying medication-related problems.[22] In the post-discharge setting, in the event that a medication reconciliation may take a considerable amount of time, literature suggests that there may not be a difference between early versus late post-discharge follow-up, as long as the medication reconciliation and follow-up is completed within 14 days post-discharge.[23] This may allow time for pharmacists and other healthcare professionals to communicate with each other and streamline the number of post-discharge follow-ups rather than becoming overloaded with scheduling patients within the first few days.

An additional time-saving technique may be utilization of a risk-stratification score to identify high risk patients in order to provide targeted efforts for pharmacy-led TOC.[22] The Care Assessment Need score is a tool unique to U.S. Department of Veterans Affairs that involves polytomous multinomial logistic regression and predictive analytics to predict risk of hospital admission or death in primary care patients. Furthermore, using risk criteria identified in literature, a Composite Care Transitions Score (CCTS) was also used to identify patients who may benefit from pharmacist TOC interventions. This study demonstrated that these high-risk patients commonly have medication-related problems and discrepancies. Surprisingly, there was no significant difference between post-discharge in-clinic visits with regards to medication discrepancies compared to telephone follow-ups ($p = 0.41$), suggesting that phone call follow-up may be an alternative to in-clinic visits. This may be particularly useful in rural areas, where patients find it difficult to travel for a clinic appointment.[24] Since in-clinic visits can take more time to complete, this may also be a potential area to save time.

Meds-to-Beds Program Barriers

With the increasing complexity and number of patients' medication therapy, meds-to-beds programs are important to allow for bedside delivery of medications at the point of discharge. In one TOC program involving meds-to-beds program and follow-up telephone calls, the readmission rate of patients who participated in the program was only 5%, compared to 9% in usual care ($p<0.05$).[25] However, there are some potential challenges when meds-to-beds programs are initiated. Due to the complexity of these programs and the need for well-coordinated care, significant resources are needed. These can include support from a variety of stakeholders, including hospital executives, physicians, nurses, pharmacists, social workers, information technologists and any other professionals who may need to be involved in the program. After careful planning, it is recommended to start a pilot program in select high-risk patients or a specific unit in order to minimize barriers and identify solutions to problems. Regular meetings of all program leaders should be conducted to share ideas and critically solve problems that may arise.[26]

Addressing barriers through technology

Despite the various types of TOC services provided by pharmacists, inadequate communication, poor care coordination, and lack of clinician accountability still serve as barriers to effective TOC.[27] The major limitation to appropriate medication reconciliation may be the lack of communication between health care providers and pharmacies. In regards to clinician accountability, one study estimated communication occurs between inpatient and outpatient providers only 3-20% of the time, with only 12-34% of primary care providers receiving a complete discharge medication list.[28] To address this gap in communication, technological tools and innovative telecommunication may be potential solutions. In a rural setting, a community pharmacy partnered with a 95-bed hospital to provide services to patients within a 100 mile-radius. Communication was streamlined between the health care professionals and the pharmacy by the implementation of faxed discharge medication lists and electronic prescriptions.[24] Furthermore when medications were delivered to patients' homes, the delivery driver initiated videoconference calls between the patient and the pharmacist in which the pharmacist would clarify questions, discuss the new medication regimen, add OTC supplements and minerals being taken by the patient to the medication list, and remove previously prescribed medications no longer being taken by the patient. Although only 18 patients were enrolled in this pilot, the study indicated good patient satisfaction scores and 11% 30-day readmission rate (2 of 18 patients unplanned readmissions). Use of faxed medication lists, electronic prescriptions, and videoconferencing provided patients with limited access to healthcare a venue to resolve TOC medication issues. To address the concerns about fragmented communication between providers, Farris and colleagues established weekly multidisciplinary videoconference calls between the hospital and skilled nursing facilities. Via these calls, pharmacists identified 106 medication reconciliation discrepancies that were addressed by both the inpatient and outpatient providers.[29] However, the study was not able to demonstrate that the additional interventions

decreased rates of hospital readmission. Since communication to outpatient providers and pharmacists were completed via fax, further studies might prove that a verbal handoff is critical to improve patient outcomes in regards to hospital readmission.

Coding barriers:

One the biggest barriers in expanding pharmacy TOC services is the ability to fund for more pharmacists. Numerous sources of information have proven that pharmacist involvement in TOC services can provide a positive economic impact by reducing readmissions.[6] However, having the ability to bill for TOC services in the ambulatory setting can potentially serve as a direct revenue source for many outpatient clinics. Notably, CPT Code 99495 bills for "transitional care management services with moderate medical decision complexity within 14 days of discharge", and CPT Code 99496 bills for "transitional care management services with high medical decision complexity within seven days of discharge".[30] On an average, these billing codes can generate a revenue of $100 to $250 dollars.[31] Since pharmacists are not recognized as providers by CMS except when providing immunizations, pharmacists must collaborate with a licensed Medicare provider who has an established relationship with a patient in order to bill for the CPT code 99495 and 99496. Several hurdles must be overcome to generate this revenue; clinics must actively track patients discharged from the hospital and make timely follow-up phone calls and appointments with pharmacists and providers, strict documentation must be recorded, reimbursement must be sought within 30 days of patients' discharge, and patients must not be re-hospitalized within 30 days.[30] One outpatient TOC study by Trang and colleagues discussed some of these barriers as they reported only a 40.5% overall capture rate in their outpatient TOC services with a 76.7% of reimbursement for CPT codes 99495 and 99496.[32] Despite the low overall capture rate, Trang and colleagues indicated a significantly lower utilization of acute health care services in the pharmacist-led outpatient TOC group compared to the usual care group (23% vs 41.4%, p=0.013). This study identifies an area of economic benefit of pharmacist TOC services whilst delineating some of the barriers in the implementation of the services and the complexity of the CPT coding. With the increasing push for provider status and the use of technology for patient tracking, some of these barriers can be overcome. Meanwhile, further studies are warranted to explore the time and resources allocated to comply with the CMS billing regulations compared to the revenue generated from reimbursement.

Conclusion

Pharmacists focused in TOC services within multiple settings can provide substantial benefit to patient outcomes and reduce the burden of unnecessary healthcare utilization. These services can include services such as medication reconciliation, meds-to-beds programs, discharge education, post-discharge phone calls, home and clinic visits. Pharmacist involved TOC have demonstrated benefits such as reduced 30-day hospital readmission and decreased medication discrepancies in medication history and reconciliations. In order to establish high-quality TOC services, potential barriers should be identified and addressed prior to initiation of services as well as part of an ongoing quality improvement measure.

About the Authors:

Julie Kalabalik, Pharm.D., BCPS, BCCCP
Assistant Professor of Pharmacy Practice/Director for Pharmacy Practice
Fairleigh Dickinson University
juliek@fdu.edu

Sibyl Marie Cherian, Pharm.D., BCPS, BCGP
Corresponding Author
***at the time of the writing of this manuscript, the corresponding author was employed as the following:*
Clinical Assistant Professor
Fairleigh Dickinson University
sibyl.cherian@gmail.com

Malgorzata Slugocki, Pharm.D.
Assistant Professor of Pharmacy Practice
Fairleigh Dickinson University
slugocki@fdu.edu

Amulya Uppala, Pharm.D., BCPS
Clinical Pharmacist – Transitions of Care
Overlook Medical Center
amulya.uppala@atlantichealth.org

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We are grateful to the experts that review the submissions, for their recommendations greatly contribute to the quality of *The New Jersey Journal of Pharmacy*.

The Journal wish to acknowledge the following pharmacists who have participated in peer review:

Marlene Battle, BSBio, PharmD, MS
Brian Catton, PharmD
Carrie Corboy, RPh, PharmD, CCP
Brandi Duff, PharmD
Sasha Libman-Falbaum, PharmD
Harold L. Kirschenbaum, MS, PharmD
Doug Risler, RPh
Ealia Washington, PharmD, BCGP, BCACP
Ligia Westrich, Ph.D., R.Ph.

New Drug Update: Delafloxacin (BaxdelaTM) for Acute Bacterial Skin & Skin Structure Infections

Aamer Attaar, PharmD; Marc Sturgill, PharmD (Corresponding Author)
Associate Professor and Chair Department of Pharmacy Practice & Administration
Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey

Learning Objectives:

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

Pharmacist:

1. Recall specific characteristics of delafloxacin including mechanism of action, dosing, spectrum of coverage, adverse effects, and therapeutic use.
2. Analyze and interpret clinical trial data for delafloxacin as it relates to clinical relevance and pharmacokinetics..

Pharmacy Technician:

1. Recall dosing, frequency, and duration of delafloxacin administration.
2. Recognize specific compounding and storage instructions for delafloxacin.

Author disclosures: the authors have nothing to disclose
CEU Hours: 1.0 contact hour of continuing education credit (0.1 CEU)
Activity Type: knowledge based activity
UAN: 0136-0000-18-021-H04-P; 0136-0000-18-021-H04-T
Release Date: 5/25/18 Expiration Date: 5/25/21

Introduction

Fluoroquinolones encompass a large arsenal of bactericidal antibiotics used to treat a variety of Gram-positive, Gram-negative, and atypical bacterial infections. However, their use in the treatment of skin and soft tissue infections (SSTIs) is not very common. Approved in June of 2017, delafloxacin (Baxdela™, Melinta Therapeutics, Inc.) is a novel fluoroquinolone approved to treat acute bacterial skin and skin structure infections (ABSSSIs) in adults.[1]

ABSSSIs are bacterial skin infections that are at least 75 cm^2 in size based on redness, edema, or induration.[2] Types of infections include nonpurulent (necrotizing, cellulitis, erysipelas) and purulent (carbuncle, furuncle, abscess) infections.[3] Common pathogens mostly consist of Gram-positive species such as Streptococcus spp. and especially *Staphylococcus aureus*, including both methicillin-sensitive (MSSA) and resistant (MRSA). Delafloxacin was found to be non-inferior, with respect to primary outcomes, to the combination of vancomycin and aztreonam in two Phase III clinical trials in which more than half of all subjects were identified with an *S. aureus* infection.[1] Delafloxacin is also approved for the treatment of many other susceptible isolates (*Table 1)*.[1] In the absence of susceptibility testing, local epidemiology data may allow for empiric use.[1]

Approved Bacterial Isolates for Delafloxacin Use (Table 1)[1]

Type	Species
Gram-positive	• S. *aureus* (MSSA and MRSA), *Staphylococcus lugdunensis*, *Streptococcus agalactiae*, *Streptococcus anginosus*, S. *pyogenes*, E. *faecalis*.
Gram-negative	• E. *coli*, *Enterbacter cloacae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*.

Pharmacology

The molecular structures of older fluoroquinolones exhibit a positively- and negatively-charged moiety at a physiologic pH. Unlike the Zwitterionic structure of these fluoroquinolones, delafloxacin is weakly anionic at physiologic pH, and predominantly neutral at the acidic intracellular pH of bacteria.[4] This property of delafloxacin enhances bacterial uptake and inhibits egress, potentially explaining the enhanced potency of delafloxacin against methicillin-sensitive and resistant *Staphylococcus aureus*, when compared to other fluoroquinolones.[5,6] In addition to its efficacy against Gram-positive and Gram-negative

bacteria, delafloxacin also displays efficacy *in vitro* with anaerobic (*Bacteroides fragilis)* and atypical (Mycoplasma spp., Ureaplasma spp., Chlamydia spp., and *Mycobacterium tuberculosis*) species.[5]

Delafloxacin exhibits concentration-dependent bactericidal activity, via inhibition of the bacterial enzymes topoisomerase II (DNA gyrase) and IV, thereby inhibiting bacterial DNA replication, transcription, and repair.[5] In contrast to other fluoroquinolones, delafloxacin shows equal affinity for both enzymes, which may help to explain its enhanced potency and broad spectrum of activity.[5] Bactericidal activity is dependent on the ratio of the unbound delafloxacin area under the plasma concentration-time curve to the minimum inhibitory concentration (MIC of the organism (*f*AUC/MIC).[5]

Pharmacokinetics

Pharmacokinetic parameters are based on findings of three clinical studies involving a total of 94 healthy adults.[7] Following a single 60-minute, 300 mg intravenous (IV) infusion of delafloxacin, the mean ± SD peak plasma drug concentration (C_{max}) is 10.4 ± 1.95 mcg/mL, reached at a median (range) time to C_{max} (T_{max}) of 1 (0.97-1.08) hours.[7] The mean (SD) area under the plasma concentration versus time curve (AUC_{∞}) is 24.8 ± 4.87 mcg hr/mL. The apparent volume of distribution at steady-state (V_{SS}) is 34.2 ± 6.73 L.[7] Renal clearance (CL_R) is 4.98 ± 1.66 L/hour, with an elimination half-life (t½) of 8.21 ± 2.72 hours. Delafloxacin undergoes hepatic glucuronidation to inactive glucuronide metabolites.[8] The percentage of unchanged drug and glucuronide metabolites recovered in the urine, respectively, is 38.9 ± 8.92% and 20%; an additional 28.5% of the dose is eliminated in the bile as unchanged drug.[8]

The mean ± SD absolute bioavailability (F) of oral delafloxacin following a single 450 mg dose is 58.8 ± 10.5 percent.[7] The mean (SD) peak plasma drug concentration (C_{max}), reached at a median (range) time to C_{max} (T_{max}) of 0.817 (0.5-4) hours, is 6.12 ± 1.96 mcg/mL.[7] The mean (SD) area under the plasma concentration versus time curve ($AUC_{oral,\infty}$) is 24.2 ± 6.45 mcg hr/mL. A high-fat meal has no effect on the $AUC_{oral,\infty}$ of delafloxacin, although the C_{max} decreases by 20.5 percent.[9]

Clinical Trials

Delafloxacin was approved for the treatment of ABSSSIs on the basis of two multicenter, randomized, double-blind, double-dummy Phase III non-inferiority trials, involving a total of 1510 adult subjects diagnosed with ABSSSI.[10,11] Baseline characteristics consisted of a mean age of approximately 45 +/- 15 (SD) in the first trial and 50 +/- 15 (SD) in the second trial.[10,11] Subjects in both trials were also primarily Caucasian and the majority were men.[10,11] The primary endpoint for both studies was a ≥ 20% reduction in lesion size at 48 to 72 hours compared to baseline, surgical intervention, or death.[10,11] Secondary endpoints included complete resolution of signs and symptoms at 13-15 day follow-up, and presumed or documented eradication of MRSA. A non-inferiority margin of 10% and a power of 90% was established in Trial 1, while Trial 2 considered a 95% confidence interval (CI) lower limit value exceeding -0.10 as noninferior. Subjects in Trial 1 were randomized in a 1:1 ratio to receive either delafloxacin 300mg IV q12h or vancomycin 15mg/kg plus aztreonam IV q12h for 5-14 days.[10] Subjects in Trial 2 were randomized in a 1:1 ratio to receive either delafloxacin 300mg IV q12h for 3 days, followed by a mandatory switch to oral delafloxacin 450mg q12h, or vancomycin 15mg/kg IV q12h plus aztreonam for 5-14 days.[11]

Delafloxacin was non-inferior to the combination of vancomycin and aztreonam for the primary outcome—respective objective response rates of 78.2% and 80.9% in Trial 1, with a mean (95% confidence interval or CI) difference of 2.6 (-3.57 to 8.78) percent; and 83.7% and 80.6% in Trial 2, with a mean (95% CI) difference of 3.1 (-2.0 to 8.3) percent.[10,11] Delafloxacin was also considered non-inferior to the combination of vancomycin and aztreonam for complete resolution of signs and symptoms with mean (95% CI) objective response differences of -1.51 (-9.11 to 6.11) percent in Trial 1 and -2.0 (-8.6 to 4.6) percent in Trial 2.[10,11] In both trials, documented or presumed eradication of MRSA was similar and nearly 100% in both treatment and comparator arms.[10,11] Adverse drug reactions did not differ significantly, with nausea (8%), diarrhea (8%), headache (3%), vomiting (2%), liver enzyme (AST and ALT) elevation (3%) being reported most often for delafloxacin.[12]

As with all fluoroquinolones, delafloxacin has a black box warning for tendon rupture, peripheral neuropathy, and CNS effects including psychosis, convulsions, and increased intracranial pressure.[1] Other warnings include the risk of *Clostridium difficile*-associated diarrhea, exacerbation of myasthenia gravis, and the development of bacterial resistance, which can occur through mutations in bacterial topoisomerases II and IV.[1] Data for use in specific populations (*Table 2*) are limited to geriatric patients, and patients with renal or hepatic impairment.[1]

Dosage & Administration

There are three approved recommended dosing regimens (*Table 3*), all with the same dosing frequency and therapy duration.[1] Delafloxacin is available either as a single-dose vial of 300mg sterile, lyophilized powder, or as 450mg oral tablets.[1] The IV formulation should be diluted to a total volume of 250 mL of D5W or normal saline, and administered over 60 minutes.[1]

The compounded product may be stored at room or refrigerated temperature for up to 24 hours before use.[1] The oral formulation may be given without regard to food; however, as with other fluoroquinolones, it should be taken 2 hours before or 6 hours after with regard to compounds containing divalent cations, such as antacids, because of the risk of chelation and subsequent lowered bioavailability.[1]

Special Population Considerations (Table 2)[1]

Special Population	Recommendation
Pregnancy	Limited data, possible fetus ossification delay
Lactation	Insufficient data
Pediatrics	No trials done but not recommended in <18 years of age
Geriatric	Higher risk of tendonitis/rupture if ≥ 65 years old, especially with concomitant corticosteroids
Hepatic Impairment	No dose adjustment necessary
Renal Impairment	IV dose should be decreased to 200mg in patients with eGFR of 15-29 mL/min/1.73m^2

Recommended Dosing Regimens (Table 3)[1,11]

Dose	Frequency	Duration
300mg IV infusion over 60 minutes	Every 12h	5-14 days
300mg IV infusion over 60 minutes for 3 days, then switch to 450mg oral (as studied in O'Riordan et al.)	Every 12h	5-14 days
450mg oral	Every 12h	5-14 days

Summary

Delafloxacin is a unique fluoroquinolone antibiotic FDA-approved for the treatment of ABSSSIs in adults. It shows excellent *in vitro* activity against Gram-positive (including MSSA and MRSA), Gram-negative (including the Enterobacteriaceae and *Pseudomonas aeruginosa*), anaerobic, and atypical bacterial species. Due to its novel structure, delafloxacin shows enhanced potency against *S. aureus*, and maintains activity against some strains of *S. aureus* that are resistant to other fluoroquinolones. Delafloxacin should be considered an appropriate choice for the management of ABSSSIs in adult patients, especially when S. *aureus* is a likely etiology.[5] Delafloxacin may also potentially serve as an alternative in the treatment of community-acquired or nosocomial pneumonia due to excellent lung penetration observed in murine experimental models.[5,13]

About the Authors:

Aamer Attaar, PharmD
Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey
William Levine Hall, Rm. 410
160 Frelinghuysen Road
Piscataway, NJ, 08854
Phone: (848) 445-6815
Fax: (732) 445-2533
Email: aamer.attaar@rutgers.edu

Marc Sturgill, PharmD (Corresponding Author)
Associate Professor and Chair
Department of Pharmacy Practice & Administration
Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey
William Levine Hall, Rm. 410
160 Frelinghuysen Road
Piscataway, NJ, 08854
Phone: (848) 445-6815
Fax: (732) 445-2533
Email: marc.sturgill@pharmacy.rutgers.edu

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Quality Measure Gaps Targeted by RWJBarnabas Health Ambulatory Care Pharmacists

Alyssa Gallipani, PharmD, BCACP

RWJBarnabas Health is the largest not-for-profit integrated health care delivery system in New Jersey. The Ambulatory Care Division of RWJBarnabas Health is composed of two board certified pharmacists. The vision of the division is to provide integrated health services to address medication needs while developing partnerships in the community. These pharmacists practice in physician office practices within the Barnabas Health Medical Group, cumulatively with jurisdiction of over 20 prescribers. I am currently a member of the Ambulatory Care Division. My role is dedicated to building advanced pharmacy services that align with goals of these prescribers.

With the initiation of outcomes-based reimbursement by the Centers for Medicare and Medicaid (CMS), there is a shift from volume-based to value-based payment reform. CMS released the Medicare Access in Children's Health Insurance Program (MACRA) and Merit-based Payment System (MIPS), that created reimbursement models focused on the value and quality of services performed. A large portion of these quality gaps are medication related. The RWJBarnabas Health Ambulatory Care Division embraces the opportunities pharmacists have to fill these gaps, increase health system reimbursement, and optimize care.

First, we established a collaborative partnership with the one of our largest payers, a conglomerate that provides high quality care while lowering health care costs for individuals and the system. We are provided with gaps in care that if filled, would qualify the corresponding physician for reimbursement. Some medication related gaps that we have filled thus far include statin and angiotensin-converting enzyme initiation in diabetes mellitus and high-risk medication use in elderly. From January to March of 2018, over 50 gaps have been closed by a single pharmacist. By duplicating this model in the second half of 2018, we aim to improve care of other patients within the health system.

In efforts to identify other high-risk patients, we have created a dynamic worklist of patients discharged from any RWJBarnabas Health facility in the past 24 hours. This was developed to identify patients prone to medication related errors post-discharge, including Medicare patients. To fulfill the 2018 Medicare Shared Savings Program measure of medication reconciliation with 30 days post-discharge, we identify patients daily for timely follow-up. Over 25 medication related errors have been identified and resolved during this process since its implementation in January 2018. This justifies the need for additional pharmacists in the physician office practice setting.

To facilitate reporting of outcome measures, an online pharmacy reporting system was created. A list of all possible outcomes is listed for selection by the pharmacist once closed. This enables consistent reporting across the health system.

Posters of these achievements were presented throughout New Jersey, including the New Jersey Society of Health System Pharmacists Annual Meeting and Fairleigh Dickinson University School of Pharmacy Research Symposium. To increase prescriber awareness, this data has been presented to them as well. A physician has also requested to present this data alongside of the pharmacist at Saint Barnabas Medical Center to advocate for this practice model.

Overall, pharmacists can advocate for the profession by intervening on value-based measures in physician office practices. Partnerships help to identify gaps in care that can lead to gap closure, optimization of care, safe medication use, and decreased cost with increases in reimbursement. Embedding a pharmacist in physician office practices is beneficial to both patients and prescribers.

About the Author:
Alyssa Gallipani, PharmD, BCACP
alyssa.gallipani@rwjbh.org
RWJBarnabas Health, Corporate Pharmacy

Acknowledgements:
Robert T. Adamson, PharmD, FASHP- RWJBarnabas Health
Indu Lew, PharmD- RWJBarnabas Health
Jennifer Sternbach, PharmD, BCPS, BCACP-RWJBarnabas Health

Member Momentum

NJPhA member and trustee, Tony Qi, has been chosen by the PEW Charitable Trust and the National Association of Boards of Pharmacy (NABP) as the presenter and field educator for various state boards of pharmacy on the implementation and enforcement of the Drug Quality and Security Act (DQSA) to achieve the highest pharmacy practice standards. Dr. Qi has presented the training in 26 state board offices, with each training involving every field compliance officer. The presentations cover three distinct practice settings: a nuclear manufacturing facility, a retail pharmacy that conducts high-risk sterile compounding, and a medical institution. This training plays a critical role in the protection of the public health by assuring the safety, effectiveness, and security of medications for human and veterinary use in the states trained to date.

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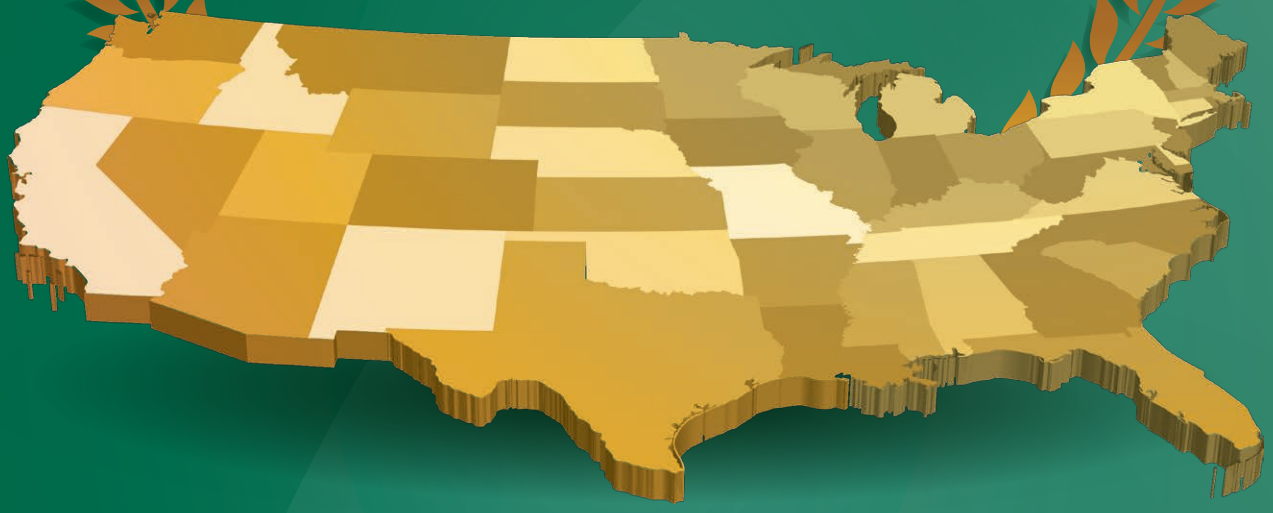

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