Urge Parents to Have Kids Vaccinated

PharmacyTimes.com
Chairman’s Note

Pharmacists Should Expect a Busy Fall

MIKE HENNESSY SR
Chairman & Founder
MJH Life Sciences™

THE DAYS ARE GETTING SHORTER, and the nights are getting colder. Students are going back to school, many of them fully masked. And pharmacists and technicians will likely have a very busy and challenging fall.

Of course, back-to-school season always means that pharmacists are swamped, dealing with an uptick in cases of head lice and sports injuries and helping parents make sure their children receive all required vaccinations.

This year will mean an added layer of pressure, however. Concern about COVID-19 variants has many on edge, and with most students now attending school in person, questions abound as to what the overall impact will be.

On August 2, 2021, the US Department of Education released guidelines for returning to school, with the message that kids need to be in classrooms.¹ The guidelines suggest that K-12 schools follow the CDC’s guidance on masking, which recommended “universal indoor masking for all teachers, staff, students, and visitors to schools, regardless of vaccination status.”²

Pharmacies, which have been on the front lines of the COVID-19 battle since the outset, are bracing for what the pandemic’s variants may bring, in part because of individuals who refuse to get vaccinated and wear masks. The delta variant, for instance, is thought to be more contagious and more serious than other versions of the virus.³

Against the backdrop of COVID-19 is the upcoming flu season, which largely did not exist last year. Some experts are expecting a difficult flu season, because immunity may have waned after a minor flu season in 2020.⁴

Any way you slice it, pharmacy staff members are likely to be extremely busy, and Pharmacy Times® will continue to provide them with the latest news and actionable information in our print publications, on our website, and in our podcasts.

In this back-to-school issue, the Cover Feature provides information on OTC treatments for allergies. Patient Focus addresses how pharmacists can help children who are being vaccinated or have missed doses. Any way you slice it, pharmacy staff members are likely to be extremely busy, and Pharmacy Times® will continue to provide them with the latest news and actionable information in our print publications, on our website, and in our podcasts.

As summer ends, we again salute pharmacists and technicians for their hard work and wish everyone a healthy and safe fall season.

REFERENCES
Advisory Board

EDITOR-IN-CHIEF
Troy Trygstad, PharmD, PhD, MBA
Vice President, Pharmacy Programs, Community Care of North Carolina

BOARD OF ADVISERS

Irfan Ali, MRPharmS
Senior Director of Network Performance
EnlivenHealth

Susan Bonilla
CEO
California Pharmacists Association

Rebecca W. Chater, MPH, RPh, FAPhA
President
Arcurus Consulting

Susan Cornell, PharmD
Professor of Pharmacy Practice/Associate Director of Experiential Education
Midwestern University

Susan M. Drelicharz, PharmD
Director of Pharmacy & Retail Ops Communications
Walgreen Co

Donna M. Feudo, RPh
Assistant Dean of Experiential Education Adjunct Clinical Assistant Professor
Ernest Mario School of Pharmacy
Rutgers, The State University of New Jersey

Kate Gainer
Executive Vice President and CEO
Iowa Pharmacy Association

Lisa M. Handley, PharmD, RPh
Senior Manager of Clinical Services
ConnectureDRX

Brian Hille, BSPharm, RPh
Senior Director, National Account Key Manager - Payer
Moderna

Michael Jackson, BSPharm, CPh
Executive Vice President/Chief Executive Officer
Florida Pharmacy Association

Nimesh Jhaveri, MBA, BSpPharm
President of Community Pharmacy and Health
Mckesson Corporation

Ronald P. Jordan, RPh, FAPhA
Dean
Chapman University’s School of Pharmacy

Anne Marie Kondic, PharmD
Executive Director
Community Pharmacy Foundation

Jessica Langley-Loep, MS
Executive Director of Education and Advocacy
National Healthcareer Association

Michael A. Manolakis, PharmD, PhD
Vice President
Aon

Allie Jo Shipman, PharmD, MBA
Director of State Policy
National Alliance of State Pharmacy Associations

Suzanne Soliman, PharmD, BCMAS
Founder
Pharmacist Moms Group

Samuel F. Stolpe, PharmD
Senior Director of Healthcare Quality Strategy
Johnson & Johnson

EDITOR EMERITUS
Fred M. Eckel, RPh, MS, ScD (Hon)
Professor Emeritus, Eshelman School of Pharmacy, University of North Carolina Executive Director Emeritus, North Carolina Association of Pharmacists

George MacKinnon III, PhD, MS, RPh, FASHP
Founding Dean and Professor
Medical College of Wisconsin’s School of Pharmacy

Michael E. McShea, RPh
Pharmacy Consultant Pharmacist
CVS

Gwendolyn McWilliams, PharmD
Senior Manager of Professional Relations
Walmart Health & Wellness

Ned Milenkovich, PharmD, JD
Principal
Much Shelist PC

Joseph Moose, PharmD
Owner
Moose Pharmacy

Tom Rhoads, MBA
Founder and Chief Executive Officer
Spencer Health Solutions, Inc
Contents

22

Cover Feature
Urge Parents to Have Kids Vaccinated
Kathleen Kenny, PharmD, RPh

Over the Counter
26 OTC Focus
Help Prevent and Relieve Allergy Symptoms
Yvette C. Terrie, BSPharm, RPh

28 OTC Product News

30 OTC Case Studies
Hypertension
Rupal Patel Mansukhani, PharmD, FAPhA, NCTTP; and Ammie J. Patel, PharmD, BCACP, BCPS

Rx Insights
33 Rx Product News

34 Rx Focus
Shingles Is a Concern at All Ages
Jeannette Y. Wick, RPh, MBA, FASCP

36 Medication Safety
Concentrations of Ibuprofen Suspensions Are Error Prone
Michael J. Gaunt, PharmD

40 Clinical Pharmacology Update
Qelbree From Supernus Pharmaceuticals, Inc
Monica Holmberg, PharmD, BCPS

Generics
41 2021 Guide to Generics

48 Generic Focus
State Legislation Aims to Improve Access to Generics
Aislinn Antrim

50 Generic Product News

» Continued on page 6

Opinions expressed by authors, contributors, and advertisers are their own and not necessarily those of Pharmacy & Healthcare Communications, LLC, the editorial staff, or any member of the editorial advisory board. Pharmacy & Healthcare Communications, LLC, is not responsible for accuracy of dosages given in articles printed herein. The appearance of advertisements in this journal is not a warranty, endorsement, or approval of the products or services advertised or of their effectiveness, quality, or safety. Pharmacy & Healthcare Communications, LLC, disclaims responsibility for any injury to persons or property resulting from any ideas or products referred to in the articles or advertisements.

August 2021 pharmacytimes.com 5
## Contents

« Continued from page 5

### Legal
52 **Pharmacy Law**  
Failure to Conduct DUR Is Basis for Negligence Suit  
Joseph L. Fink III, JD, DSc (Hon), FAPhA, BSPharm

58 **Legislative Focus**  
Telehealth Proves of Great Value During COVID-19  
Elizabeth H. Bernauer and Joseph L. Fink III, JD, DSc (Hon), FAPhA, BSPharm

### Pharmacy History
60 **Pharmacy History**  
Heart Drug Has an Intriguing Past  
Karen Berger, PharmD

### Independent Corner
62 **Independent Corner**  
Corner Drug Is a Thriving Multigenerational Family Business  
Karen Berger, PharmD

### Consultation Counter
64 **Technician Focus**  
There Is More to Medication Storage Than Meets the Eye  
Stephanie Majercak, CPhT

66 **Patient Focus**  
Managing Medications at School Is More Than a Family Affair  
Alexandra Bieniek

### Condition State Management
68 **Health & Wellness**  
International Overdose Awareness Day Is Somber Reminder  
Christopher Epps

### OTC Product News
28

### Rx Product News
33

### Generic Product News
50

» Continued on page 8
Contents

Continuing Education
77 Individualized Care for Patients With Immune Thrombocytopenia: The Role of the Pharmacist
At the completion of this activity, the participant will be able to:

• Examine immune thrombocytopenia (ITP) pathophysiology, clinical presentation, and impact on patient quality of life
• Analyze the latest data on the efficacy, safety, dosing, and administration of current treatment options for ITP
• Demonstrate the pharmacist’s role in the management of patients with ITP

88 Risks of Respiratory Syncytial Virus in Older Adults: Emerging Prophylactic Vaccines and Intervention Opportunities for Pharmacists
At the completion of this activity, the participant will be able to:

• Determine the pathology, symptomatology, and diagnosis of respiratory syncytial virus (RSV)
• Explore the latest information on the safety, efficacy, administration, and dosing of the emerging vaccines for RSV
• Examine the role of the pharmacist in the management of RSV, including adult patient education on current preventive methods and emerging vaccines

103 Advancing Treatment of Chronic Kidney Disease in Patients With Diabetes: Key Considerations for Pharmacists
At the completion of this activity, the participant will be able to:

• Identify the epidemiology of diabetes and chronic kidney disease (CKD) as well as the pathology of kidney disease in this patient population and the impact of inflammation and fibrosis as a progressive factor
• Analyze current guidelines for CKD and type 2 diabetes (T2D) and the clinical trial data surrounding the emerging nonsteroidal mineralocorticoid receptor antagonists in treatment
• Illustrate the impact of pharmacists in coordination of care and treatment strategies for CKD in patients with T2D
This month on social media, we wanted to know why you became a pharmacist.

Carmen O.: I grew up watching my mother being one, so that became an inspiration for me.

Sohail M.: To understand humans better.

Nnaka U.: I always loved health care, but knew that I didn’t want to be a medical doctor (I hate the hospital environment and can’t spend the rest of my life working at a hospital). So being a pharmacist became the next natural option.

CB: Always knew I wanted to go into medicine, but not as a physician/nurse/PA. I liked that pharmacy is a more independent part of the system and the longer I practice the more I love it. I started toward clinical but really enjoy being part of the community by working retail.

Youssef: Pharmacy is like the bridge between chemical/biological sciences and medicine; this is what I love most about pharmacy.
Editor’s Note

Expect Explosive Growth in Specialty Pharmacy and the Neo-Pareto Rule of 80/2

You Read That Correctly; Drop the Zero in 20 to Explain Spending in the Sector in the Near Future

By TROY TRYGSTAD, PHARMD, PHD, MBA, EDITOR IN CHIEF

12% of Fills Were Greater Than 50% of the Cost in 2020, Soon to Become 80%

If categorization is based on expense, perhaps it is no surprise that specialty pharmacy represents more than half of all drug spending in the United States, projected to be more than $500 billion within 2 years.1 By 2025, 2% of all prescription fills will represent at least 80% of the total cost of medications. That eventuality is staggering and has tectonic implications for the pharmacy sector.

Specialty Pharmacy Locations Are Growing, but They Are Not Your Parents’ Community Pharmacies

Between 2015 and 2019, the number of accredited specialty pharmacy locations in the United States grew to 1069, from 381.2 However, a disproportionate number of these pharmacies were not remote call centers with dispensing by mail, but rather a mix of courier, local, and mail, resulting from an influx of health systems seeking 340B margins and an increasing need for near-site or on-site services for specialty prescribers. All the while, the average community pharmacy was getting squeezed out of the marketplace by carry costs, limited distribution, and narrow networks. Specialty pharmacies are largely call center–based care delivery, with specialized knowledge of disease states but also complex coverage circumstances and rules, spending much of their personnel’s time on approval and revenue cycle management.

Vertical Integrations Prompted by the Ability to Capture Specialty Utilization and Manage Internally

The past decade brought about inevitable vertical integrations among insurers, pharmacies, pharmacy benefit managers (PBMs), and third-party administration functions. The advantages are obvious. If a pharmacy needs only to channel 2% of prescriptions to itself and capture 80% of the market, it can have a “market” without an actual marketplace or market dynamics. And the pharmacy can play both sides of the channel: the consumer, through positioning of out-of-pocket costs, and the manufacturer, through demanding more rebates.

Without a solid categorical definition, specialty pharmacy’s generally accepted criterion is that drugs are expensive.

Some medications require special handling; some special knowledge about administration, adverse effects, conditions, and contraindications; and others are just pills to be taken twice daily, no differently from most small-molecule pharmaceuticals.

“Specialty” medications have no generally accepted definition for categorization, largely because the insurers and their contracted pharmacy benefit managers want to separate them by their most meaningful difference from other therapeutics: cost. Specialty products can be treated differently with respect to data collection, networks, provider reimbursement, and rebates. It is all too tempting to use pricing as the principal criterion for categorizing a medication as “specialty.”

TROY TRYGSTAD, PHARMD, PHD, MBA, is vice president of pharmacy provider partnerships for Community Care of North Carolina, which works collaboratively with more than 2000 medical practices to serve more than 1.6 million Medicaid, Medicare, commercially insured, and uninsured patients. He received his PharmD and MBA degrees from Drake University and a PhD in pharmaceutical outcomes and policy from the University of North Carolina. He also serves on the board of directors of the American Pharmacists Association Foundation and the Pharmacy Quality Alliance.
Doubling Down on Certain Specialty Drugs: Cigna’s “Shared Savings” Program for Patients

Cigna recently announced a “shared savings” program for generic biologicals, in which patients can be given a $500 debit card by choosing the biosimilar. This consumer incentive becomes an even more powerful negotiating chip when asking competing brand manufacturers for additional rebates, some of which are passed along to the plan and some kept by the pharmacy benefit manager. Playing both sides of the table has positioned the middlemen to control nearly all the drug spending because specialty makes up the majority and is managed under a different set of rules than nonspecialty, which means tighter control of providers.

Health Systems Buckle Down on 340B and Specialty; New Lexicon Develops on “Bag Color”

It is no secret that 340B programs have started to replace disproportionate share hospital (DSH) proceeds as the most important revenue generator to backfill the coffers of health systems that provide care to low-income and uninsured patients. DSH dollars are allocated through the states from the federal government via Medicaid to the tune of $19.7 billion in 2019, with a large number of hospitals receiving tens of millions of dollars in the program. The Affordable Care Act contained provisions to reduce the program size because Medicaid expansion was meant to reduce uncompensated care, but legislation over the years has chipped away at the reductions. Regardless, for some health systems, 340B proceeds now exceed DSH payments.

The importance of keeping 340B prescriptions in-house to the bottom line of health systems cannot be overstated. Simply put, 340B is now the “opioid epidemic” of health systems, which are completely dependent on the program to protect against layoffs and reduced service delivery system-wide, not just with pharmacy divisions. Between manufacturers attempting to reign in contract pharmacies and “white bagging”—wherein the payer is the dispenser to the site of care, leaving the latter to administer the drug to patients but not receive the buy-sell margin—health systems are on high alert regarding specialty pharmacy distribution and reimbursement channels. Specialty medications have become the payer-policymaker-provider battleground of the future.

Specialty products can be treated differently with respect to data collection, networks, provider reimbursement, and rebates.

Will the Bifurcation of Pharmacy Practice and Cost Structures Lead to a Different Payment Model for Community Pharmacy?

Netting out mail order and specialty pharmacy, community pharmacies likely represent approximately 75% of the prescription fills but between 10% and 15% of the total spending within a few years. So why the pressure to reduce reimbursement to communities if their dispensing will represent such a small part of the overall cost of drug spending?

It begs the question: Should there be separate reimbursement models for nonspecialty and specialty pharmacy, with nonspecialty pharmacy reimbursed solely on services rather than product?

There are more than 300 medications on the market that cost essentially nothing per pill. Why spend so much energy and administrative money on maximum allowable cost and state maximum allowable cost, direct and indirect renumeration fees, and all the other spreadsheet nonsense? Why not simply pay only for the services provided? A fair day’s reimbursement for a fair day’s care of patients: pay for services, not for medications that cost next to nothing. No nonsense needed.

REFERENCES

## FDA Approvals

### Biologics License Applications, Biosimilars, Generics, and New Drug Applications

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Indication</th>
<th>Manufacturer</th>
<th>Date approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asparaginase erwinia chrysanthemi (recombinant) rywn (Rylaze)</td>
<td>Indicated for the treatment of acute lymphoblastic leukemia or lymphoblastic lymphoma in pediatric patients ages 1 month and older and adults who have developed hypersensitivity to E coli-derived asparaginase, and as a component of a multiagent chemotherapeutic regimen</td>
<td>Jazz Pharmaceuticals</td>
<td>6/30/21</td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda)</td>
<td>Indicated as monotherapy in adults with recurrent, metastatic, or locally advanced cutaneous squamous cell carcinoma that is incurable by surgery or radiation</td>
<td>Merck Pharmaceuticals</td>
<td>7/6/21</td>
</tr>
<tr>
<td>Enfortumab vedotin-ejfv (Padcev)</td>
<td>Indication expanded to include adult patients with locally advanced or metastatic urothelial cancer who are ineligible for cisplatin-containing chemotherapy and have previously received 1 or more prior lines of therapy</td>
<td>Astellas</td>
<td>7/9/21</td>
</tr>
<tr>
<td>Finerenone (Kerendia)</td>
<td>Indicated to reduce the risk of kidney function decline, kidney failure, cardiovascular death, nonfatal heart attack, and hospitalization for heart failure in adults with chronic kidney disease associated with type 2 diabetes</td>
<td>Bayer Healthcare</td>
<td>7/9/21</td>
</tr>
<tr>
<td>Daratumumab and hyaluronidase-fihj (Darzalex Faspro)</td>
<td>Indicated in combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma following their first or subsequent relapse</td>
<td>Janssen Pharmaceuticals</td>
<td>7/12/21</td>
</tr>
<tr>
<td>Pneumococcal 15-valent conjugate vaccine (Vaxneuvance)</td>
<td>Indicated for the prevention of invasive pneumococcal disease caused by 15 serotypes in adults 18 years of age and older</td>
<td>Merck Pharmaceuticals</td>
<td>7/16/21</td>
</tr>
<tr>
<td>Dexamethasone and tobramycin ophthalmic suspension 0.3%/0.1%</td>
<td>Indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists</td>
<td>Amneal Pharmaceuticals, Inc</td>
<td>7/19/21</td>
</tr>
<tr>
<td>Immune globulin intravenous (human) 5% (Octagam)</td>
<td>Indicated for use in adults with dermatomyositis</td>
<td>Octapharma USA</td>
<td>7/20/21</td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda)</td>
<td>Indicated in combination with lenvatinib for the treatment of advanced endometrial carcinoma that is not microsatellite instability-high or mismatch-repair deficient, and for patients who have experienced disease progression following prior systemic therapy in any setting but who are not candidates for curative surgery or radiation.</td>
<td>Merck Pharmaceuticals</td>
<td>7/22/21</td>
</tr>
<tr>
<td>Zoster vaccine recombinant, adjuvanted (Shingrix)</td>
<td>Expanded indication for the prevention of herpes zoster in adults 18 years and older who are, or will be, at an increased risk of shingles because of immunodeficiency or immunosuppression</td>
<td>GlaxoSmithKline</td>
<td>7/26/21</td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda)</td>
<td>Indicated for the treatment of patients with high-risk early-stage triple-negative breast cancer in combination with chemotherapy as a neoadjuvant treatment, and then continued as a single agent after surgery</td>
<td>Merck Pharmaceuticals</td>
<td>7/27/21</td>
</tr>
<tr>
<td>Insulin glargine injection (Semglee)</td>
<td>The first interchangeable biosimilar insulin product for patients with type 1 or type 2 diabetes mellitus</td>
<td>Mylan Pharmaceuticals Inc</td>
<td>7/28/21</td>
</tr>
<tr>
<td>Mepolizumab (Nucala)</td>
<td>Indicated as a treatment for patients with chronic rhinosinusitis with nasal polyps</td>
<td>GlaxoSmithKline</td>
<td>7/29/21</td>
</tr>
<tr>
<td>Selexipag injection (Uptravi)</td>
<td>Indicated for the treatment of pulmonary arterial hypertension in adult patients with WHO functional class II-III who are temporarily unable to take oral therapy</td>
<td>Janssen Pharmaceuticals</td>
<td>7/30/21</td>
</tr>
</tbody>
</table>

For the full FDA approvals list, go to pharmacytimes.com.
CDC Recommends Vaccinated Individuals Wear Masks Indoors in Areas With High Transmission Rates

THE CDC UPDATED ITS COVID-19 GUIDELINES, urging vaccinated individuals in areas of high and substantial transmission to wear masks in public indoor spaces, including schools, to prevent the spread of the delta variant.1

The CDC recommends that all individuals in K-12 schools wear a mask indoors, including all staff members, students, and visitors, regardless of vaccination status. Further, the organization urged community leaders in areas of high transmission to encourage universal masking and vaccination to help prevent the spread of the delta variant.1

Recent data suggest that in rare occasions, vaccinated individuals infected with the delta variant after vaccination may be contagious and spread the virus to others. However, there is a greater risk of infection from unvaccinated individuals, according to the CDC.

The Infectious Diseases Society of America released a statement in support of the new guidelines, citing statistics underlying the low rates of vaccination throughout the United States. Vaccination coverage is below 40% in more than half the counties in the country, and 63% of US counties have high or substantial virus spread, according to CDC data.2—Skylar Kenney

Pfizer, BioNTech Provide Additional Vaccine Doses, Extend Clinical Trials

PFIZER INC AND BIONTECH SE are providing an additional 200 million COVID-19 vaccines to the United States, according to a statement and will be expanding their clinical trials of the vaccines in children aged 5 to 11 years.2

The additional doses are expected to be delivered between October 2021 and April 2022, bringing the total number of doses to 500 million.1

These doses were provided under the companies’ existing supply agreement with the US government and are in addition to the 500 million doses expected to be provided for donation to the world’s poorest nations.1

The companies plan to deliver 110 million of the additional doses by December 31, with the remaining 90 million doses expected by April 30, 2022. The government also has the option to acquire updated versions of the vaccine that could address potential variants, if authorized and available.1

In addition to purchasing the additional doses, government agencies have urged Moderna and Pfizer-BioNTech to expand the size of their clinical trials among children aged 5 to 11 years. This expansion is part of an effort to detect rare adverse effects in this patient population, including heart inflammation problems that have been seen in individuals 30 years and younger.2

FDA officials think the scope of the original trials was inadequate to detect the adverse effects. Because of this, the FDA has asked the companies to include 3000 children aged 5 to 11 years, which is approximately double the original number of study participants planned.2—Aislinn Antrim

Remdesivir Is Linked to Reduction in Mortality Rate in Hospitalized Patients

THREE ANALYSES OF LARGE, retrospective, real-world data sets have found that remdesivir was associated with a reduction in mortality rates in patients hospitalized with COVID-19, according to a statement from Gilead Sciences, Inc.

Remdesivir is indicated for hospitalized adults and pediatric patients 12 years and older who weigh at least 40 kg for the treatment of COVID-19.

The 3 data analyses include 98,654 patients hospitalized with COVID-19. Two of the studies observed treatment trends and outcomes in the United States using the HealthVerity and Premier Healthcare databases, and the third analysis compared clinical outcomes in patients receiving a 10-day treatment course of remdesivir in the extension phase of the SIMPLE-Severe study.

This reduction in mortality was observed across a spectrum of baseline oxygen requirements, and the results were consistent at different time frames over the course of the pandemic and across geographic regions, according to the investigators.

Results of 2 of the studies also showed that patients who received remdesivir had a significantly increased chance of discharge from the hospital by day 28.

The analysis of data from HealthVerity assessed 24,856 patients treated with remdesivir versus matched controls (n = 24,856) between May 1, 2020, and May 3, 2021.

Investigators found that in the overall population, patients receiving remdesivir had a statistically significant 23% lower mortality risk than patients in the control arm, regardless of baseline oxygen requirement.

Investigators also observed a significantly greater likelihood of discharge by day 28 in patients who completed a full 5-day course of remdesivir compared with patients in the control arm. This result was most pronounced in patients with lower oxygen requirements at baseline.

Similarly, an analysis of data from the Premier Healthcare Database found that patients treated with remdesivir had a significantly lower risk of mortality at days 14 and 28 versus patients who did not receive remdesivir.—Aislinn Antrim
Weekly Injection of Efpeglenatide Shows Reduction in Cardiorenal Events in Patients With T2D

NEW FINDINGS FROM AN INTERNATIONAL, large-scale clinical trial have found a significant reduction in the first occurrence of a heart attack, stroke, or death and a reduction in progression of kidney disease in patients with type 2 diabetes (T2D) who received a weekly injection of efpeglenatide.

The new data were presented at the 81st Scientific Sessions of the American Diabetes Association (ADA) and simultaneously published in the New England Journal of Medicine.

Efpeglenatide is an injectable drug with glucose- and weight-lowering effects. The majority of adults (98%) with T2D have at least 1 comorbid chronic condition, such as cardiorenal conditions that affect the heart and kidneys. Specifically, 22% individuals living with diabetes have cardiovascular disease, 82% have hypertension, and 24% have kidney disease, according to the ADA.

Efpeglenatid, a GLP-1 receptor agonist (GLP-1 RA), is used to treat diabetes by reducing blood pressure, glucose levels, and weight. Previous research has shown that GLP-1 RA drugs based on human GLP-1 benefit cardiovascular and kidney outcomes. The AMPLITUDE-O trial (NCT03496298) assessed the impact of a GLP-1 RA based on exendin-4, either with or without an SGLT2 inhibitor drug, in patients with cardiovascular or kidney disease. The clinical trial was conducted in 28 countries and included more than 4000 patients with T2D.

Over 2 years, patients who received weekly injections of efpeglenatide versus a placebo had a 27% lower risk of a heart attack, stroke, or cardiovascular death, according to the ADA. Furthermore, investigators found a 32% lower risk of kidney disease progression and a 27% lower risk of death, heart attack, or stroke from any cause in the efpeglenatide arm.—Aislinn Antrim

Investigational Treatment for Alzheimer Disease Reports Positive Top-line Clinical Data

THE INVESTIGATIONAL THERAPY BIIB080/IONIS-MAPTRX (Biogen, Inc and Ionis Pharmaceuticals, Inc) met its primary objective of safety and tolerability in patients with mild Alzheimer disease (AD) in a phase 1b placebo-controlled, multiple ascending-dose clinical study, according to a statement from Biogen.

The study results further demonstrated robust time and dose-dependent lowering of tau protein in cerebrospinal fluid (CSF) during the 3-month treatment period, and these reductions were sustained over the 6-month posttreatment period.

Until recently, the treatment of AD was limited to symptom management.

Growing evidence suggests that aggregated, hyperphosphorylated tau may be a key driver of neurodegeneration in AD, in addition to other tauopathies including progressive supranuclear palsy and frontotemporal degeneration, according to the investigators.

BIIB080 is an investigational antisense therapy designed to target microtubule-associated protein tau messenger RNA and prevent production of tau protein.

Dose-dependent decreases in the concentration of total tau in CSF were seen in patients receiving BIIB080 8 weeks after the final dose.

Mean percentage reduction of 30%, 40%, and 49% were seen in the low-, medium-, and high-dose groups treated every 4 weeks, respectively, and 42% in the group treated every 12 weeks. —Skylar Kenney

Women, Black Adults Are Less Likely to Receive Heart Failure Diagnoses in Primary Care Settings

STUDY FINDINGS PUBLISHED IN Circulation: Heart Failure show that many heart failure diagnoses in the primary care setting may be missed in women, Black adults, and individuals with lower net worth. These individuals are significantly more likely to receive a heart failure diagnosis in an acute care setting, such as during hospitalization or in an emergency department.

This discrepancy remains even if the individual reported symptoms of heart failure during a routine outpatient health care appointment within the past 6 months, according to the investigators.

The study was conducted using a national database of commercial insurance and Medicare Advantage health care claims from 2003 to 2019.

The investigators evaluated whether patients with new incidence of heart failure were diagnosed in an acute care or outpatient setting and included nearly 1 million adults 18 years or older with a first-time heart failure diagnosis.

According to the investigators, 38% of patients with newly diagnosed heart failure received their diagnosis in an acute care setting. Further, 46% of those patients had symptoms of potential heart failure during a primary care clinic visit within the previous 6 months, including edema (15%), cough (12%), chest pain (11%), and shortness of breath (11%). These acute care diagnoses were more common among women than men and also more common among Black adults compared with White adults.

Additionally, individuals with a net worth below $25,000 had 39% higher odds of receiving heart failure diagnoses in an acute care setting.—Skylar Kenney
Education, Training Are Essential for Successful Flu Vaccination Campaigns

Experts Anticipate a Return to High Influenza Rates as COVID-19 Prevention Measures Decline

By AISLINN ANTRIM

AS MEDICAL PROFESSIONALS PREPARE FOR the first flu season following the COVID-19 pandemic, educating patients about the importance of vaccination and training pharmacy technicians about effective communication are essential to the mass vaccination campaign starting in the fall.

Two recent Pharmacy Times® The Perfect Consult® videos explored the roles that pharmacists and technicians play in flu vaccination campaigns.

Pharmacists are ideally positioned to educate patients about the impact of influenza on public health and the need for flu vaccinations.

The flu causes up to 45 million illnesses, 810,000 hospitalizations, and 61,000 deaths annually, according to data from the CDC.1

Although the figures were significantly lower in the 2020-2021 season because of protection measures taken during the COVID-19 pandemic, vaccination ahead of the 2021-2022 season is no less important.

In addition to the impact on public health in general, influenza poses significant risks for individuals with comorbidities or who are older. For example, approximately 80% of annual flu-related deaths occur among older adults, and individuals with diabetes account for approximately 30% of adult flu-related hospitalizations.2

Pharmacy staff members have myriad opportunities to encourage flu vaccinations when speaking with patients. For example, when dispensing medications for diabetes or other comorbidities, pharmacists can ask whether patients have received flu vaccinations. Automated systems may also inform staff members if patients have not yet received their vaccinations.

Some patients may think the COVID-19 vaccine protects them from the flu. It is important to point out that although the number of flu cases in 2020 was significantly lower than usual, this was most likely due to hand-washing, mask wearing, and social distancing. In addition, pharmacists should point out that flu shots are strongly recommended every year, especially for older adults with chronic health conditions.

Furthermore, the results of a recent study show that the influenza vaccine may lower patients’ odds of testing positive for COVID-19 as well as reduce the burden of disease in patients who have received a virus diagnosis.3

The population at higher risk of flu-related complications is also at the greatest risk of COVID-19, so increasing vaccinations in this group is paramount.

In addition to educating patients about the necessity of flu vaccinations, training technicians on how to have these conversations is essential to the success of an immunization program.

Encouraging flu vaccinations while patients are receiving their COVID-19 vaccinations or booster shots can be a convenient way to have these conversations.

As pharmacy offerings have increased, technicians have stepped up to support these new services, including immunizations. They are frequently the first point of contact at the pharmacy, giving them opportunities to engage with patients, identify potential immunization services, and initiate the process for the patient to consult with a pharmacist or receive a vaccination.

Collaboration among pharmacy staff members can have a significant impact on immunization rates and disease prevention.
When speaking with patients at the pharmacy counter, technicians can explain that flu vaccinations are especially important as COVID-19 safety precautions decline. Experts expect flu rates to rise as mask and social distancing regulations end, so vaccination is especially important ahead of the 2021-2022 flu season.

Sharing reliable information from the CDC and other sources can also help educate patients about the importance of flu vaccinations. Technicians can also recommend that patients speak with a pharmacist if they have more clinical questions about the flu vaccine, and these consults can occur while patients are picking up prescriptions to ensure a convenient, quick option.

Allowing technicians to drive immunization efforts and engage with patients also positively affects the business needs of the pharmacy. However, to do this, technicians must have the education and training to empower them for these situations.

Because pharmacists are managing multiple activities and responsibilities, using the skills of technicians can be incredibly beneficial. Not all patients coming into a pharmacy need to speak with a pharmacist, so technicians can be a valuable resource, especially at the point of sale.

REFERENCES
Urge Parents to Have Kids Vaccinated

CDC Publishes a Schedule of Recommended Immunizations, How Many Doses Are Required, and at What Age They Should Be Administered

Babies are born with immune systems that can fight off most germs, but there are some serious diseases that they cannot fend off.
These diseases once harmed or killed infants, children, and adults. Fortunately, vaccines can provide immunity from these diseases without having to get sick. Certain vaccines have even eradicated some diseases.

Childhood vaccinations also help others stay healthy, thanks to herd immunity or community immunity. This is particularly important for individuals who cannot get certain vaccines because of their age, allergies, or being immunocompromised.

The CDC publishes a vaccine schedule that includes recommended vaccines, how many doses are required, and at what age they should be administered.¹

INFANTS AND TODDLERS: AGED BIRTH THROUGH 2 YEARS

Vaccines contribute to a healthy start in infants and toddlers. Some of these vaccines may require more than 1 dose to boost and build immunity and include the following:²

- Chickenpox (varicella) vaccine: given at aged 12 to 15 months
- DTP vaccine: given at aged 2 months, 4 months, 6 months, and 15 to 18 months
- Flu vaccine: recommended every year by the end of October starting at aged 6 months
- *Haemophilus influenzae* type b vaccine: given at aged 2 months, 4 months, 6 months (if needed, depending on the brand), and 12 to 15 months
- Hepatitis A vaccine: given at aged 12 to 23 months and again 6 months after the first dose
- Hepatitis B vaccine: given shortly after birth, at aged 1 to 2 months, and at 6 to 18 months
- Measles-mumps-rubella (MMR) vaccine: given at aged 12 to 15 months; infants aged 6 to 11 months should receive 1 dose before traveling abroad.
- Pneumococcal vaccine: given at aged 2 months, 4 months, 6 months, and 12 to 15 months
- Polio (IPV) vaccine: given at aged 2 months, 4 months, and 6 to 18 months
- Rotavirus vaccine: given aged 2 months, 4 months, and perhaps 6 months, depending on the brand

PRESCHOOL AND ELEMENTARY SCHOOL: AGED 3 THROUGH 10 YEARS

Children need additional doses of some vaccines at this age. A certificate of childhood immunizations may be required for school enrollment. These vaccines include the following:²

- Chickenpox (varicella) vaccine: given aged 4 to 6 years
- DTaP vaccine: given aged at 4 to 6 years
- Flu vaccine: recommended every year by the end of October
- IPV vaccine: given at aged 4 to 6 years
- MMR vaccine: given at aged 4 to 6 years

PRETEENS AND TEENS: AGED 11 THROUGH 18 YEARS

Adolescents need additional vaccines because some childhood vaccines lose their protection over time. Adolescents also need protection from additional diseases before the risk of exposure increases. These vaccines include the following:³

- If a child leaves the country, check to see if he or she needs additional vaccinations.
- Flu vaccine: recommended every year by the end of October
- Human papillomavirus vaccine: given at aged 11 to 12 years and again 6 to 12 months after the first dose
- Meningococcal conjugate vaccine: given at aged 11 to 12 years and again at aged 16 years
- Serogroup B meningococcal vaccine: may be given at aged 16 to 23 years
- DTP vaccine: given at aged 11 to 12 years

MANDATING VACCINES

Vaccines are mandated at the state level. Each state can decide which vaccines to mandate and when. However, to be mandated at the state level, vaccines must be fully approved by the FDA. Most states mandate vaccines for children to allow them to attend charter, private, and public schools as well as day care programs.³

If a child has a job, his or her employer can require a COVID-19 vaccination, even though these vaccines have only been approved for emergency use by the FDA. Employers can do this because attendance is not compulsory. They have the right to require vaccinations, regardless of whether they are fully approved, and workers have the right to refuse and find another job.⁴

EXEMPTIONS TO MANDATED VACCINES

Just as mandated vaccines are handled at the state level, so are the exemptions. All states and the District of Columbia allow a medical exemption to vaccination. This occurs when a child has a medical condition that prevents him or her
from receiving a vaccine. All but 3 states offer nonmedical exemptions for philosophical or religious reasons. Philosophical reasons include objections to vaccines based on moral, personal, or other beliefs.5

An exemption in school vaccination assessment reports could mean several things, such as the parent refused all vaccines for the child, the parent refused a dose of vaccine for the child, or the parent refused a specific vaccine series for the child.5

States vary in their requirements to apply for exemption. Some require annual reenrollment for exemption, and others require a certification of completion of an online educational model. These requirements are changing. Some states are adding more vaccinations to the required list, and some are removing nonmedical exemptions. Advise parents to contact the local school board or state department of health for more information.

PREPARE FOR A POSITIVE EXPERIENCE
Immunizations can be stressful for both the child and the parent. It is important for parents to stay calm because children are sensitive to the emotions of their caregivers. Parents should answer questions honestly and use terms that may lessen anxiety. During the appointment, they can use varying techniques to keep children calm and distracted.

Some parents premedicate their child with acetaminophen or ibuprofen to lessen the aftereffects of an immunization. Advise parents to check with pediatricians performing the immunization to determine whether they feel this is helpful and to get an appropriate dose. ■

REFERENCES

HELPFUL RESOURCES

- CDC 2021 recommended vaccinations for children (aged 7-18 years)
  https://www.cdc.gov/vaccines/schedules/easy-to-read/adolescent-easyread.html

- CDC 2021 recommended vaccinations for infants and children (aged birth to 6 years)
  https://www.cdc.gov/vaccines/schedules/easy-to-read/child-easyread.html

- CDC child and adolescent vaccine assessment tool
  https://www2a.cdc.gov/vaccines/childquiz/

- American Academy of Physicians childhood vaccines: What they are and why your child needs them

- CDC for parents: Vaccines for your children
  https://www.cdc.gov/vaccines/parents/index.html

- US Department of Health & Human Services vaccine basics
  https://www.hhs.gov/immunization/basics/index.html

- CDC COVID-19 vaccine information
  https://www.vaccines.gov/
In a few weeks, students and teachers across the country will begin returning to the classroom to start a new school year. Although back-to-school season is exciting, individuals heading back to the classroom who are prone to allergies often face numerous challenges. Symptoms present with varying degrees of severity and often negatively affect an individual’s quality of life by causing fatigue and sleep disturbances and impairing concentration. Allergy symptoms also often contribute to absences from school and work and a loss of productivity.

For individuals who suffer from seasonal allergies, finding relief from the common symptoms, such as headaches, itchy and watery eyes, nasal congestion, and repetitive sneezing, is a top priority. Unfortunately, the selection of a nonprescription allergy product can be overwhelming, particularly for individuals who have other medical conditions and/or take other medications. Pharmacists can be instrumental in guiding patients in the selection and proper use of nonprescription allergy products and directing them to seek further medical care when warranted. Prior to initiation of pharmacologic therapy, a patient’s medical and medication history should be thoroughly assessed to determine whether self-treatment is appropriate and to prevent contraindications and drug interactions.

During this time of year, ragweed pollen is responsible for most symptoms associated with fall allergies.1-4 With 17 species of ragweed pollen, peak levels typically occur in mid-September, affecting an estimated 23 million individuals in the United States.2

Almost 75% of individuals who are allergic to spring plants also experience allergic reactions to ragweed.1-3 Ragweed pollen can also aggravate asthma symptoms, which can lead to coughing and wheezing.2 Other plant allergens that trigger fall allergy symptoms may include mugwort, sagebrush, and tumbleweed.

Other possible causes of fall allergy symptoms include dust mites and mold.2,4,5

Moreover, the American College of Allergy, Asthma, & Immunology (ACAAI) indicates that some students present with allergy symptoms in the fall because of exposure to allergens in the classroom, such as chalk dust and classroom pets.6

A study published in the Annals of Allergy, Asthma & Immunology, the scientific journal of the ACAAI, found that 75% of adults with asthma aged 20 to 40 years and 65% of adults with asthma aged 55 years and older have at least 1 allergy.7

Available OTC products for the self-treatment and prevention of mild to moderate allergy symptoms include intranasal corticosteroids (INCS), mast cell stabilizers, ocular and oral antihistamines, and oral and topical decongestants. INCS have been shown to be the most effective treatment for most of the symptoms associated with allergic rhinitis.8 Pharmacists can also be
instrumental in recommending dosage forms that are convenient and easy to use, such as long-acting, once-daily formulations and/or orally disintegrating tablets, especially for pediatric patients.

**RECENT NEWS**

In June, the FDA approved azelastine hydrochloride nasal spray 0.15% (Astepro Allergy; Bayer) as an OTC product for the temporary relief of itchy nose, nasal congestion, runny nose, and sneezing associated with upper respiratory allergies such as hay fever. Its recent approval makes it the first steroid-free antihistamine nasal spray for indoor and outdoor allergies available over the counter in the United States.

OTC Astepro Allergy is indicated for use in patients 6 years and older. Each nasal spray delivers a volume of 0.137-mL solution containing 205.5 μg of azelastine hydrochloride. The product may be administered as a once- or twice-daily dosage regimen. The OTC formulation includes flexible dosing that provides up to 24-hour relief from itchy nose, nasal congestion, runny nose, and sneezing caused by indoor and outdoor allergies.

Because of the risk of somnolence associated with the use of azelastine, the label for Astepro Allergy warns consumers to avoid alcoholic drinks and to be cautious when driving a motor vehicle or operating machinery. Additionally, consumers should avoid sedatives or tranquilizers when using the product.

The 0.15% strength is approved for OTC use, but the 0.1% strength will remain prescription based for perennial and seasonal allergic rhinitis. The manufacturer anticipates that Astepro Allergy will be available at national mass retail locations the first quarter of 2022.

**ROLE OF THE PHARMACIST**

Pharmacists can assist patients who suffer from allergy symptoms in the selection and proper use of nonprescription products. They can also provide patients with key information about the most efficacious nonpharmacological and pharmacological measures to prevent or reduce allergy symptoms. Masks have been used to reduce transmission of COVID-19, but some study results have shown that masks may also be helpful in reducing allergy symptoms.

During counseling, patients should be advised to use OTC products as recommended and be aware of potential adverse effects.

Patients experiencing severe allergy symptoms should be encouraged to seek further care from their primary health care provider. They can also make recommendations about patient education resources that teach patients about back-to-school allergy plans such as the Allergy & Asthma Network website (https://allergyasthmanetwork.org/health-a-z/covid-19/covid-19-school-resources-for-managing-asthma-and-allergies/) and the ACAAI website (https://www.aaaai.org/tools-for-the-public/conditions/library/asthma/back-to-school-with-allergies-and-asthma).

**REFERENCES**

BeautiCap Hair Vitamins
Manufactured by BeautiCap by Dr Sankar
These capsules contain carefully selected antioxidants and vitamins proven to help strengthen hair follicles and grow strong hair. They contain ascorbic acid, biotin, cyanocobalamin, folate, riboflavin, and vitamin A, and they are cruelty and gluten free, as well as vegan. A pharmacist with an interest in nutrition and its impact on beauty developed these supplements, which are effective in both men and women.

FOR MORE INFORMATION:
beauticapvitamins.com

Nourishing Hand Wash, Hand Sanitizer
Manufactured by Dove
Dove is entering the hygiene space with its new Deep Cleansing Hand Wash, Foaming Hand Wash, and Hand Sanitizer. All the products aim to remove germs while moisturizing and nourishing skin. Notably, the hand sanitizer is 99.99% effective against germs, keeps skin moisturized for up to 8 hours, and is available in scents such as shea butter with warm vanilla and lavender with yogurt.

FOR MORE INFORMATION:
dove.com

Humble CBD
Manufactured by Humble Specialty Products, LLC
Humble Specialty Products has launched a new line of cannabidiol (CBD) products for busy lifestyles that includes a balm, chewables, a dropper, single-serve oil drops, and softgels. The Humble CBD Balm is 1000 mg of CBD in a roll-on. The chewable is available in 750-mg or 1000-mg dosages, and the softgels are available in 900 or 1000 mg. The dropper comes in 3 strengths and 8 flavors, and the single-serve oil drops are 33 mg of CBD per serving and available in 4 flavors. The line is marketed to “skaters, surfers, snowboard enthusiasts, and beyond as an option to incorporate into their wellness regimens,” according to a company news release.

FOR MORE INFORMATION:
humblebrands.com

GoodSkin MD
Manufactured by Procter & Gamble
With science-backed products formulated for sensitive skin, Procter & Gamble’s new GoodSkin MD line features 6 hypoallergenic skin care products proven to help improve skin resiliency and reduce the effects of stress on skin. The collection includes a brightening serum with vitamin C complex, a facial cleanser to remove dirt and oil without drying the skin, a facial moisturizer with zinc oxide sunscreen (sun protection factor 15), a night cream to strengthen the skin’s natural barrier, a rescue cream to smooth imperfections, and a smoothing serum with vitamin B complex.

FOR MORE INFORMATION:
getgoodskinmd.com
OTC Cases

Hypertension

By RUPAL PATEL MANSUKHANI, PHARMD, FAPHA, NCTTP; AND AMMIE J. PATEL, PHARMD, BCACP, BCPS

RUPAL PATEL MANSUKHANI, PHARMD, FAPHA, NCTTP, is a clinical associate professor at Ernest Mario School of Pharmacy at Rutgers, The State University of New Jersey in Piscataway, and a transitions-of-care clinical pharmacist at Morristown Medical Center in New Jersey.

AMMIE J. PATEL, PHARMD, BCACP, BCPS, is a clinical assistant professor of pharmacy practice and administration at Ernest Mario School of Pharmacy at Rutgers, The State University of New Jersey in Piscataway, and an ambulatory care specialist at RWJBarnabas Health Primary Care in Shrewsbury and Eatontown, New Jersey.

AUTHOR BIOS

CASE 1: Decongestants

Q

GR, aged 38 years, has had congestion for the past few days and wants something to help open her airways. She says she usually uses pseudoephedrine but was recently diagnosed with high blood pressure (HBP), which she is trying to control through diet and exercise. Her blood pressure (BP) readings for the past week have been 138-156/90-98. GR does not take other medications. What should the pharmacist recommend?

A

Pseudoephedrine can be used as a decongestant. However, it can cause a slight increase in BP. In patients with controlled hypertension, the results of one metaanalysis showed that BP increased by 1 mm Hg. Patients who took higher doses had even higher increases. Because GR has uncontrolled BP, she should avoid pseudoephedrine. Patients with hypertension should use decongestants only if advised to do so by their physicians, and they should monitor their BP during use. OTC products that are marketed for patients with hypertension often do not include decongestants. GR can try to use a dehumidifier and nasal saline and see whether her congestion improves.

CASE 2: BP Monitoring

Q

HH is a 48-year-old man looking for a BP monitor. He was recently diagnosed with hypertension, and his physician recommended that he monitor his BP at home. HH is looking for a wrist monitor because he wants a small device that is portable for work. He takes hydrochlorothiazide 25 mg and lisinopril 10 mg daily for HBP. HH is otherwise healthy. What should the pharmacist recommend?

A

The American Heart Association recommends home monitoring for all patients with HBP to help assess and modify treatment. Finger and wrist BP monitors are not recommended because the readings may not be reliable. When choosing a monitor, it is important to assess appropriate cuff size; the cuff bladder should encircle 80% or more of the patient’s arm circumference. HH should be seated comfortably with his back supported, a bare upper arm, and his legs uncrossed. Advise him not to drink caffeine, exercise, or smoke 30 minutes before measuring his BP. It is also important to take the reading at a similar time each day to see trends. HH can take his BP multiple times throughout the day to assess whether his medications are working. He should be familiar with his goal BP and contact a health care professional if the reading is elevated.

» Continued on page 32
OTC Cases

« Continued from page 30

**CASE 3: DASH Diet**

**Q**

LM is a 55-year-old woman who would like a multivitamin. She was recently diagnosed with hypertension. LM was prescribed 2 medications, but her physician said she should also diet and exercise. Her medications include amlodipine 5 mg and losartan 50 mg daily and atorvastatin 20 mg at bedtime. LM began going to a gym a few days a week but is having trouble adhering to a diet and is tired of eating salads. She asks about a diet that can help reduce her BP. What should the pharmacist recommend?

**A**

The Dietary Approaches to Stop Hypertension (DASH) diet can help patients reduce their BP level. DASH recommends eating fruits, vegetables, and whole grains instead of refined grains. In addition, the diet suggests incorporating beans, fat-free or low-fat dairy products, fish, nuts, poultry, and nontropical vegetable oils to replace foods that are high in saturated fat, such as fatty meats, full-fat dairy products, and tropical oils (coconut, palm kernel, and palm oils). LM should also limit sugar-sweetened drinks and sweets. In addition, encourage her to limit her salt intake to less than 2300 mg daily, or approximately 1 teaspoon, because data show that less than 1 teaspoon of salt per day can lower BP by 2 to 8 mm Hg. However, if LM can tolerate less than 1500 mg per day, her BP will likely be even lower. LM should also speak with a dietitian to assess daily caloric intake and learn how to read food labels.

**CASE 4: Stevia**

**Q**

GG is a 48-year-old woman who wants to refill her medication for lisinopril 10 mg daily. She has had hypertension for 5 years but has been able to control it with diet, exercise, and medication. A friend suggested GG use stevia instead of sugar in her coffee because it can lower BP. Should she try the stevia to help control her hypertension?

**A**

Advise GG that the data are conflicting regarding the use of stevia for hypertension. The results of 1 study showed that taking stevioside, a constituent of stevia, had a 12 mm Hg mean reduction in systolic BP and an 8 mm Hg reduction in diastolic BP. However, results of another study showed no reduction in BP when using stevioside in doses up to 15 mg/kg daily. Although stevia has conflicting data, its safety profile is relatively safe. Therefore, if GG wants to use stevia in her coffee, she can certainly try it. Advise her to monitor her BP daily and contact a health care professional if it increases.
Pneumococcal 20-valent Conjugate Vaccine (Prevnar 20)
Manufactured by Pfizer Inc
The FDA recently approved Pfizer’s new 20-valent conjugate vaccine for the prevention of invasive disease and pneumonia caused by the 20 Streptococcus pneumoniae serotypes in adults 18 years and older. The vaccine includes capsular polysaccharide conjugates for the 13 serotypes already included in Prevnar 13, plus conjugates for 7 additional serotypes shown to cause invasive pneumococcal disease and linked to antibiotic resistance, high case-fatality rates, and meningitis.

FOR MORE INFORMATION:
Pfizer.com

Olanzapine and Samidorphan Tablets (Lybalvi)
Manufactured by Alkermes, Inc
Patients with bipolar I disorder or schizophrenia have a new once-daily treatment option since the recent FDA approval of olanzapine and samidorphan tablets as a maintenance monotherapy for the acute treatment of manic or mixed episodes or as an adjunct to lithium or valproate. In the ENLIGHTEN-2 clinical development program, the novel antipsychotic demonstrated efficacy, safety, and tolerability, with patients taking Lybalvi reporting significantly less weight gain than patients taking olanzapine alone. The approval is based on data from 27 clinical studies, including 18 studies evaluating Lybalvi and 9 studies evaluating samidorphan alone.

FOR MORE INFORMATION:
alkermes.com

Semaglutide Injection (Wegovy)
Manufactured by Novo Nordisk
Semaglutide injection was recently approved for use with a reduced calorie meal plan and increased physical activity to help stimulate weight loss in adults with obesity or who are overweight and also have weight-related medical problems. It is the only prescription weight-loss medication with once-weekly dosing, according to a company statement. Results from the STEP 1 (NCT 03548935) trial found that patients taking semaglutide injections achieved an average weight loss of 14.9% of body weight at 68 weeks versus 2.4% for patients receiving a placebo. The most frequently reported adverse events for patients using semaglutide were abdominal pain, constipation, diarrhea, nausea, and vomiting.

FOR MORE INFORMATION:
novonordisk-us.com

Tapinarof Cream
Manufactured by Dermavant Sciences
The FDA is considering approval for Dermavant’s novel, once-daily topical tapinarof, indicated for the treatment of mild, moderate, and severe plaque psoriasis in adults. The therapeutic aryl hydrocarbon receptor modulating agent inhibits proinflammatory mediators associated with inflammation. Two phase 3 trials established its efficacy, with data showing that tapinarof met all primary and secondary end points and demonstrated a similar safety profile consistent with previous clinical trials. Overall, it was well tolerated, with a 5.8% discontinuation rate due to adverse events.

FOR MORE INFORMATION:
dermavant.com

FOR MORE INFORMATION:
dermavant.com
**SHINGLES, A VARICELLA-ZOSTER VIRUS (VZV)** infection of an individual nerve and the associated skin surface, is diagnosed by its defining characteristic: rash along a nerve path. Yet patients complain more about unbearable pain, often describing a sensation of electrical shock and small needles against the skin with muscle pain.

Individuals with shingles find any touch, even from clothing, extremely painful.

Approximately 1 in 3 Americans will develop shingles, which translates to 1 million cases annually. Pain can begin 2 to 4 days before the rash appears, and severe pain can persist as postherpetic neuralgia (PHN). Patients with PHN report burning, shooting, stabbing, and/or throbbing pain. Other symptoms include chills, loss of or decreased hearing or vision, fever, gastrointestinal upset, headache, muscle weakness, scarring, or skin infection. Herpes zoster ophthalmicus (HZO) is a growing concern. An analysis of 21 million adults showed that HZO tripled during a 12-year period from 9.4 cases per 100,000 people to 30.1 cases per 100,000 people. HZO can lead to blindness and corneal scarring.

**WHO IS AT RISK?**

Shingles is uncommon but not unknown in children. Risk increases with age, especially after 40. Individuals 60 or older are 10 times more likely to develop shingles than a 10-year-old. Hospitalization for complications occurs in 1% to 4% of individuals with shingles, with the immunosuppressed and older adults at greatest risk.

Although VZV causes both chicken pox and shingles, they differ. Chicken pox is a mild illness that mainly affects children and then remains dormant in the body's central nervous system. Shingles results from viral reactivation when a trigger weakens the immune system. Investigators suggest several triggers (Box 1).

Approximately half of all shingles cases occur in individuals older than 60 and half in younger individuals, although shingles seems to be increasing in the latter group. Here, too, immunocompromise increases the risk.

Shingles does not recur in most individuals, but it can recur a second and, rarely, a third time. After an outbreak, the risk of recurrence is initially lower than the risk of a first outbreak in shingles-naive people. However, within 7 years, recurrence risk approaches 5%, which is similar to the risk of first-time shingles. In addition to immunocompromised individuals, patients who experienced severe shingles-related pain lasting more than 30 days and women are at greatest risk of recurrence. Recurrences usually affect a different part of the body.

A cancer diagnosis of any kind in any age group has been linked to a 40% increase in risk for developing shingles. Patients with hematological cancer have been associated with a 3-fold higher risk.
and the risk appears to be present 2 years prior to the diagnosis.

Solid tumors also increase the risk (but slightly less than hematological cancer) and often while the patient is receiving chemotherapy, which is immunosuppressing.10

DISEASE MANAGEMENT

Individuals who have active shingles can pass the virus to others who never had chicken pox or who are not vaccinated.11 When blisters are present, direct contact with fluid from blisters can spread VZV. The CDC recommends avoiding scratching or touching the rash, covering the rash, and washing hands often. It also recommends avoiding contact with individuals who are immunocompromised, low–birth-weight or premature infants, and pregnant women who have never had the chicken pox or the varicella vaccine.11

Vaccinating children with the chicken pox vaccine and adults 60 and older with the recombinant zoster vaccine (RSV; Shingrix) is the best prevention. Children who receive the varicella vaccine are significantly less likely to contract pediatric shingles,11 and RSV reduces the risk of developing shingles by approximately 50% and significantly reduces the likelihood of serious complications.5

Antiviral drugs, such as acyclovir, famiciclovir, or valacyclovir, reduce the length and severity of a shingles outbreak if started within the first 3 days. Clinicians can also prescribe duloxetine or nortriptyline, 8% capsaicin (Qutenza) skin patches for affected areas, lidocaine skin patches, gabapentin or pregabalin, or opioids.9

Keeping the rash clean and dry reduces infection risk. Patients should avoid antibiotic adhesive or topical dressings, use products such as calamine lotion to relieve and soothe itching, and wear comfortable, loose-fitting clothing.1

CONCLUSION

To understand shingles better, investigators are conducting studies but need healthy individuals and those with shingles to volunteer. While we wait for better preventive methods and treatments, educating patients with facts about shingles can help them protect themselves against the condition and its complications. ■

REFERENCES


BOX. Factors That May Trigger Shingles1,4

- Cancer or its treatments
- Children of mothers who had chicken pox late in pregnancy
- History of chicken pox
- Immunosuppressing comorbidities
- Medications, especially immunosuppressive drugs
- Older age
- Stress or trauma
PARENTS WHO ARE TOLD TO give their child or infant OTC ibuprofen oral suspension may not be aware that 2 different concentrations are available.

An infant’s formulation (for infants aged 6-23 months or weighing 5.5-10.5 kg or 12-23 lbs) contains 50 mg/1.25 mL (40 mg/mL). This is twice as concentrated as the children’s formulation (for children aged 2-11 years or weighing 10.9-43.1 kg or 24-95 lbs), which contains 100 mg/5 mL (20 mg/mL). Community pharmacies, grocery stores, and mass merchandisers routinely stock both concentrations. Also, the labeling and packaging of the 2 concentrations can sometimes look similar.

Staff members at pediatric hospitals might be familiar with this and have often made a point of educating parents about this issue at discharge. However, for many reasons, staff members have informed the Institute for Safe Medication Practices (ISMP) about mix-ups that sometimes occur after discharge. One reason is that some hospital computer systems sometimes convert oral liquid doses to a metric volume to help parents measure each dose using a dosing cup or oral syringe. However, the concentration parents might already have at home or purchase is often unknown.

One hospital reported a close call involving a child who was discharged from an ambulatory-surgery unit. The child’s mother was concerned because she was familiar with giving her child (who weighed 8.6 kg) less than 2 mL of ibuprofen, as per the manufacturer’s label instructions. The discharge instructions, however, said to give 4.3 mL, or 86 mg of the 100-mg/5-mL concentration. After confirming that the mother had the 50-mg/1.25-mL concentration at home and not the 100-mg/5-mL concentration, the hospital was able to tell the mother the appropriate volume of ibuprofen to administer to her child for each dose.

In another case, a child was prescribed ibuprofen 70 mg every 6 hours. The child’s mother was told to give 3.5 mL of the medication for each dose, with the expectation that the 100-mg/5-mL suspension would be used. However, the child’s mother purchased ibuprofen suspension 50 mg/1.25 mL (200 mg/5 mL) and gave her child the 3.5 mL per dose as instructed. So instead of receiving 70 mg, the child received 140 mg per dose.

Fortunately, we are not aware of any serious adverse outcome resulting from this 2-fold overdose, but the possibility of adverse effects is likely...
increased. An overdose might lead to diarrhea, headache, kidney damage, nausea, stomach bleeding, and vomiting.

This situation is similar to an issue that has since been resolved with oral liquid acetaminophen (Tylenol) products, which, for many years, existed in 2 concentrations: a less concentrated liquid (160 mg/5 mL) for children and a more concentrated liquid (100 mg/mL) for infants.

When the 100-mg/mL concentration was accidentally administered to children in volumes appropriate for the 160-mg/5-mL product, there were accidental deaths and serious injuries to children. Faced with this evidence, manufacturers voluntarily withdrew the more concentrated infant product and agreed to only provide the 160-mg-per-5-mL concentration that is available today (some manufacturers label their products as 500 mg/15 mL).

Because of the potential for harm and the continuing nature of these ibuprofen errors, the ISMP has asked the FDA to look into the matter to determine whether the more concentrated product is necessary. One of the children’s hospital nurses who spoke with the ISMP queried colleagues about this, and the overwhelming response was, “Why isn’t there just 1 concentration of liquid ibuprofen similar to acetaminophen?”

Ideally, Johnson & Johnson Consumer Health, the original sponsor of Children’s Motrin (ibuprofen) for children aged 2 to 11 years, would modify the infant concentration to match the children’s concentration as was done for acetaminophen, with other ibuprofen manufacturers to follow.

For now, the ISMP recommends that health care providers counsel parents about the availability of the 2 liquid ibuprofen strengths and that the 100-mg/5-mL strength includes “children’s ibuprofen” in the name and the more concentrated 200-per-5-mL (50 mg/1.25 mL) strength is referred to as “concentrated infant drops.”

Also be sure that parents understand that the dose in mL (volume) must be based on which concentration they are using.

FIGURE. Dosing errors have occurred when parents and practitioners mix up children’s ibuprofen (100 mg/5 mL), left, and infant concentrated ibuprofen (50 mg/1.25 mL), right.
Qelbree From Supernus Pharmaceuticals, Inc

By MONICA HOLMBERG, PHARMD, BCPS

THE FDA HAS APPROVED QELBREE (viloxazine extended-release capsules; Supernus Pharmaceuticals, Inc) for the treatment of attention-deficit/hyperactivity disorder (ADHD) in pediatric patients aged 6 to 17 years.1

ADHD is one of the most common mental health conditions in the United States. Qelbree is a nonscheduled, nonstimulant medication.2

PHARMACOLOGY AND PHARMACOKINETICS

Qelbree is a selective norepinephrine reuptake inhibitor. Its mechanism of action in the treatment of ADHD remains unclear.

Qelbree reaches steady-state plasma concentration after 2 days of once-daily oral administration. The median time to peak plasma concentration is approximately 5 hours, with a range of 3 to 9 hours, after a single dose of 200 mg. Qelbree is mainly metabolized by CYP2D6, UGT1A9, and UGT2B15. It displays a mean elimination half-life of approximately 7 hours. Its primary route of excretion is renal.1

DOSE AND ADMINISTRATION

The recommended starting dose of Qelbree for patients aged 6 to 11 years is 100 mg orally, once daily. The dose may be titrated in 100-mg increments at weekly intervals to the maximum recommended dose of 400 mg, once daily. Patients aged 12 to 17 years should begin treatment with 200 mg orally, once daily. The dose may be increased by 200 mg after 1 week of treatment to the maximum recommended dose of 400 mg, once daily. Patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73m²) should begin treatment with 100 mg, once daily, with titrations in 50-mg to 100-mg increments at weekly intervals to the maximum recommended dose of 200 mg, once daily. A dose adjustment is not required for patients with mild to moderate renal impairment (eGFR, 30-89 mL/min/1.73m²). Dose titrations should be based on patient response and tolerability.

Qelbree may be taken with or without food. The capsule may be swallowed whole or opened and sprinkled entirely onto a teaspoonful of applesauce, which should be completely consumed without chewing within 2 hours. The capsules should not be chewed, crushed, or cut.1

CLINICAL TRIALS

Qelbree was evaluated for efficacy in the treatment of ADHD in 3 double-blind, multicenter, parallel group, placebo-controlled, randomized, short-term monotherapy trials of pediatric patients aged 6 to 17 years with ADHD. Study 1 consisted of participants aged 6 to 11 years. After a 1-week titration period, participants received once-daily Qelbree 100 mg or 200 mg or a placebo for the 5-week maintenance phase. Study 2 consisted of participants aged 6 to 11 years. After a 3-week titration period, participants received once-daily Qelbree 200 mg or 400 mg or a placebo for the 5-week maintenance phase. Study 3 consisted of participants aged 12 to 17 years. After a 1-week titration period, participants received once-daily Qelbree 200 mg or 400 mg or a placebo for the 5-week maintenance phase.

The primary end point of each study was the change from baseline in the total score on the ADHD Rating Scale 5 (ADHD-RS-5), which assesses symptoms of hyperactivity, impulsivity, and inattentiveness. A secondary end point was the Clinical Global Impression-Improvement (CGI-I) score. Each study found a statistically significant greater reduction in the ADHD-RS-5 total score and CGI-I score in the participants who received either dose of Qelbree versus those participants who received the placebo.1

CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

Qelbree carries a boxed warning stating that higher rates of suicidal behaviors and thoughts were reported in pediatric patients with ADHD who were using Qelbree than in those who received a placebo. All patients using Qelbree should be closely monitored for clinical worsening and for the emergence of suicidal behaviors and thoughts.

Concomitant administration of Qelbree with monoamine oxidase inhibitors (MAOI) or the use of Qelbree within 14 days after discontinuing an MAOI is contraindicated. Concomitant use of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range with Qelbree is also contraindicated.

Blood pressure and heart rate should be assessed prior to beginning treatment, following each dose increase, and periodically thereafter. Patients should be screened for bipolar disorder before beginning the medication. Caution is advised when driving or operating hazardous machinery because of the potential for fatigue, lethargy, sedation, and somnolence while using Qelbree. Qelbree should not be used during pregnancy or in patients with hepatic impairment.

The most common adverse reactions were decreased appetite, fatigue, insomnia, irritability, nausea, somnolence, and vomiting.1

FOR REFERENCES, GO TO PHARMACYTIMES.COM/PUBLICATIONS.
Generics Can Reduce Spending on Diabetes Drugs
Savings for These Medications Range From 40% to 75.8%, Study Results Show

By AISLINN ANTRIM

Findings from a prospective study of diabetes treatments published in the *International Journal of Advanced Research in Medicine* show that the trend of increasing expenditure can be reduced with the use of generic drugs.1

Diabetes is the reason for a growing proportion of national health care budget increases worldwide, as the number of patients increases. It is projected to become a main global cause of death and disability within the next 25 years, and experts urge immediate action to find cost-effective treatment strategies.1

For this reason, investigators in India conducted a prospective study over 6 months to better understand the variations between branded diabetes drugs and generic options, including other complications of type 2 diabetes. Investigators included participants in populations ranging from adolescents to geriatrics and analyzed data on the patients’ reasons for admission, various clinical conditions for which drugs were prescribed, which drugs were prescribed, and cost.1

A total of 1800 patients were included, ranging from younger than 20 years to age 100 years. Hypertension was noted in approximately 45% of cases, hypothyroidism in 2% of participants, and peripheral neuropathy in 5%. Diabetic retinopathy and lower limb cellulitis were both observed in 1% of cases.1

In a price comparison for the most commonly prescribed branded and generic drugs, the investigators found significant savings for patients prescribed the generic options. For example, a generic metformin 50 mg had a 40% savings compared with the branded version. This was the lowest savings, however, with differences as high as 75.8% for the other generics.1

The combination of vildagliptin 50 mg and metformin 500 mg were between 70% and 71.7% less expensive than their branded counterparts, and glitazide 80 mg plus metformin 500 mg had the greatest savings at 75.8%.1

Savings such as these can have a massive impact both on national health care expenditures and on patients. Because of its chronic nature and the frequent occurrence of comorbidities, the paper authors said that medications account for a large portion of the direct cost of diabetes.1

Other research has found that prescribing generic or preferred medications can improve adherence for patients with chronic conditions. The results of a study published in *JAMA Internal Medicine* showed that patients who initiated therapy with generic and preferred medications had 62% and 30% greater odds, respectively, of achieving adequate adherence compared with patients who received nonpreferred medications.2

Prescribing generic drugs is one way to lower medication costs in chronic care, but the biggest barrier to generic drug adoption is patient and physician skepticism about their efficacy and quality. Policymakers can play a major role in encouraging adoption, with policies designed to encourage use of generics and increased education for prescribers.

Patients with diabetes spend a large percentage of income on managing their disease, according to the study authors. In addition to minimizing expenditures for larger health systems and these patients individually, dispensing generic medications whenever possible can improve medication adherence and disease outcomes.1

REFERENCES
Alembic Pharmaceuticals, Inc in Bridgewater, NJ is a subsidiary of Alembic Pharmaceuticals Ltd., the oldest pharmaceutical company in India, employing more than 12,000 people. Alembic Pharmaceuticals, Ltd. is one of the most well-respected, established, and integrated pharmaceutical companies in Asia and supplies products to over 90 countries across the globe. Alembic Pharmaceuticals Ltd. is listed on the Bombay Stock Exchange under the stock symbol (APLLTD). Alembic is a vertically integrated organization with expertise spanning across the entire pharmaceuticals value chain: Research & Development, Manufacturing and Marketing of finished dosage formulations, as well as active pharmaceutical ingredients and intermediates.

RESEARCH AND DEVELOPMENT A KEY STRENGTH
Alembic’s strong growth and success is built on a foundation of strong and innovative R&D. In FY 2021, Alembic invested 12.4% of sales into R&D with over 90% focused on ANDAs for the U.S. market. With two research facilities in India (Vadodara and Hyderabad) and one in the U.S. (West Caldwell, NJ) and a team of over 1,200 scientists, Alembic has been a leader in development of active pharmaceutical ingredients, generic drug formulations (ANDAs), and new chemical entities. Alembic currently boasts 117 Drug Master Files (DMFs), 128 approved ANDAs, 16 Tentative Approvals and 1 NDA – 505(b)(2) as well as 212 ANDAs filed in total. In addition, Alembic has a 150-patient bed FDA approved bio-equivalence center to support ANDA filings.

STATE OF THE ART FACILITIES
Alembic supplies products from 5 FDA approved facilities in India (1 solid oral finished dose, 1 dermatology facility and 3 API facilities). These facilities have supplied product to the US market for over 10 years and include products such as Aripiprazole, Febuxostat, Pregabalin, and Valsartan. These facilities are in compliance with standards of the US FDA, UK MHRA and TGA Australia amongst others and all have been recently inspected by US FDA.

US FOCUS AND GROWTH
Alembic Pharmaceuticals Ltd. via its subsidiary Alembic Pharmaceuticals, Inc. has identified the U.S. as its key focus market. Alembic has experienced tremendous growth in the U.S. since its first launch in October 2015 and at print sells 89 products in the U.S. representing more than 330 SKUs under its own label. Alembic has continued to expand its product offering and now offers solid oral, dermatology, ophthalmic products covering a broad range of indications. For 2021 Alembic plans to launch 15+ generic products in the US market. In total, Alembic has 250+ ongoing product projects for the US market. Alembic has also completed construction of an Oncology injectables and has submitted products from approval for this facility. A second solid oral dose facility has also been completed and awaiting final FDA approval which will provide new products and redundancy for existing products.

“It’s very exciting to be part of such a dynamic organization that is focused on growth and servicing our customers and ultimately patients” said Eric Purcell, Vice President of Sales and Marketing at Alembic Pharmaceuticals, Inc.

For more information, visit alembicusa.com.
Alembic for the Long Run

- Oldest Pharmaceutical Company in India Established in 1907
- Vertically Integrated on Over 90% of Our Products
- Over 86 Product Launches since October 2015
- Over 250+ SKUs
- Robust Pipeline of over 100 ANDAs in Various Dosage Forms

750 Route 202 • Bridgewater, NJ 08807 USA
Tel: 908-393-9604 • Fax: 908-393-9605 • Email: info@alembicusa.com • alembicusa.com
Amring Pharmaceuticals Inc.

**AMRING PHARMACEUTICALS INC.** was born of a long legacy of trust, respect, and success. The company’s mission is to ensure that patients have seamless, timely access to high-quality niche generic and value-driven brand medications while providing excellent customer service at a reasonable cost.

Amring is a subsidiary of SEVER Life Sciences B.V., a global private specialty pharmaceutical company based in the Netherlands. Amring is partnered with well-established global biopharmaceutical companies, enabling it to leverage their expertise in bringing biotechnology derived medicines, sterile manufacturing, and other state-of-the-art technologies to the marketplace.

With focus on supplying specialized and unique products in targeted markets, Amring offers a simple value proposition to customers, partners, and the pharmaceutical marketplace: Leverage every opportunity to meet specific customer demands with value-added medicines. The company’s customer service is second to none. The team forges relationships based on flexibility, trust, and personal attention because they realize your patients cannot wait for the medicines they need. Every day they keep in mind the fact that you serve patients.

Amring has strategically positioned itself to make and market affordable products. The company is well invested in the success it has achieved with desmopressin acetate and tranexamic acid. Its expanded generic portfolio also includes arsenic trioxide, succinylcholine chloride, and mesalamine suppositories. Amring is always actively seeking to enhance its portfolio and takes pride in the success of the suite of product varieties—from tablets and suppositories to injectables—that it offers to its customers.

The company’s leadership team brings noteworthy experience in generic pharmaceuticals and related industries. Amring’s senior pharmaceutical executives have proven success in building businesses from the ground up, a keen ability to quickly maximize global resources at a local level, and the commitment and experience to support long-term, sustainable relationships. The company’s broad capabilities can also fill the gaps in pharmaceutical development, manufacturing, marketing, and distribution.

Backed by a notable heritage of accomplishment in the pharmaceutical industry, Amring is poised to continue its growth by bringing more significant, high-quality pharmaceutical products to the marketplace.

For more information, visit amringusa.com.
You serve patients.  
We serve you a consistent supply of generic products.

<table>
<thead>
<tr>
<th>Product</th>
<th>Dose</th>
<th>Pack Size</th>
<th>NDC</th>
<th>Brand Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desmopressin Acetate Tablets</td>
<td>0.1 mg</td>
<td>100 Count</td>
<td>69918-101-01</td>
<td>† Authorized Generic to DDAVP®</td>
</tr>
<tr>
<td></td>
<td>0.2 mg</td>
<td>100 Count</td>
<td>69918-201-01</td>
<td>† Authorized Generic to DDAVP®</td>
</tr>
<tr>
<td>Desmopressin Acetate Solution for Injection</td>
<td>4 mcg/mL</td>
<td>1 x 10 mL Vial</td>
<td>69918-901-10</td>
<td>† Authorized Generic to DDAVP®</td>
</tr>
<tr>
<td>Mesalamine Suppositories</td>
<td>1000 mg</td>
<td>30 Count</td>
<td>69918-560-30</td>
<td>AB to Canasa®</td>
</tr>
<tr>
<td>Tranexamic Acid Tablets</td>
<td>650 mg</td>
<td>30 Count</td>
<td>69918-301-30</td>
<td>Authorized Generic to Lysteda®</td>
</tr>
</tbody>
</table>

You Serve Patients. We Serve You.

Interested in learning more about Amring? Visit our website at amringusa.com

Rx Only
The Amring Logo and the “A” Logo are trademarks of Amring Pharmaceuticals, Inc.
Amring Pharmaceuticals Inc. / 1205 Westlakes Dr., Suite 275, Berwyn, PA 19312 / 844.304.4828 / www.amringusa.com
© 2021 Amring Pharmaceuticals Inc. 0620214881 PM21-012
Camber Pharmaceuticals, Inc

Camber is committed to continuous supply in generics
The past 18 months have been the most challenging in memory, and Camber has done everything possible to provide uninterrupted access to all our essential medicines. In the face of numerous challenges, our parent company, Hetero Drugs of India, has worked tirelessly to maintain the integrity of our supply chain while also leading the fight against COVID-19 worldwide.

Hetero was the first company to launch the licensed generic version of remdesivir in the Indian pharmaceutical market under the brand name Covifor™. Hetero is producing over 100 million doses of the Sputnik V COVID-19 vaccine per year in India; it is the world’s first registered vaccine against the novel coronavirus infection. Hetero is continually adding to its manufacturing capabilities, including its own KSMs (key starting material), and has more than doubled tech transfers between facilities to ensure continued production of both APIs (active pharmaceutical ingredient) and finished doses.

Vertically integrated global resources
We have achieved many of the goals we set for ourselves at the beginning of 2021 in impressive fashion. Among them are building and maintaining an abundant inventory of safety stock on many items that our customers depend on most. We have also completed our new headquarters and warehouse facility, greatly expanding our capabilities. We utilize our global resources to bring value as a trusted and reliable trading partner.
VERTICALLY INTEGRATED FROM PIPELINE TO PATIENT

When one of the world’s largest API manufacturers is your parent company, quality, value and supply are strengths you can count on.

We’re Camber.
We deliver peace of mind.

FROM PIPELINE TO PATIENT

EXPANDING AND DIVERSIFYING OUR PORTFOLIO
Long known for being leaders in antiviral and antiretroviral products, Hetero and Camber will soon be launching a comprehensive portfolio of oncology products. Having recently launched several injectable products, Camber has added a variety of dose forms to our product line, including suppositories, ointments, and suspensions.

CAMBER CONSUMER CARE, OUR OTC DIVISION
Camber Consumer Care has recently introduced several new products to our growing portfolio of allergy, pain, and gastroenterology products, including loratadine, omeprazole, and polyethylene glycol. Our mission is to provide a focused and reliable supply of over-the-counter drugs to the marketplace, creating value for our partners and savings for the consumer. Our vision is to become a strategic supplier to retailers demanding a quality-driven, reliable, and responsive OTC store brand source.

Camber goes the extra mile to understand the dynamics and concerns facing our customers. From sales to finance, from customer service to supply chain, the people of Camber foster high-touch relationships across all departments of your organization. Camber is committed to customer service and continuous supply. We value your partnership.

For more information, visit camberpharma.com.
Generic Focus

State Legislation Aims to Improve Access to Generics

Washington State’s House Bill 5203 Allows Health Care Authority to Partner With Other Agencies to Produce, Distribute, and Purchase the Drugs

By AISLNN ANTRIM

WITH THE RECENT PASSAGE OF Senate Bill 5203 (SB 5203), Washington has become the latest state trying to improve access to generic drugs.

Washington Governor Jay Inslee signed SB 5203 into law on May 12. The law authorizes the Washington State Health Care Authority (HCA) to partner with other states, nonprofits, and state agencies to produce, distribute, and purchase generic drugs.

It also requires state-purchased health insurance programs to procure generic drugs through the partnership, according to a statement from Senator Kevin Van De Wege, who sponsored the bill.

“It’s common knowledge that Americans pay far more for everyday prescription drugs than our neighbors to the north and south,” he said in the statement. “People shouldn’t have to go broke paying for common drugs like insulin instead of the less costly, generic alternatives commonly available in other countries.”

The law specifies that all drugs must be produced or distributed by a drug company or generic drug manufacturer registered with the FDA and requires that any HCA partnership result in savings for purchasers and consumers. Furthermore, health carriers, local governments, private entities, and others may purchase generic drugs from the HCA when availability allows.

“The higher prices Americans pay for medications that cost far less in other countries is a national disgrace,” Van De Wege said. “This long-overdue legislation will free up money for other important household needs, at least for folks here in Washington.”

Notably, the law allows the HCA to forge partnerships to purchase and distribute name-brand insulin to ensure accessibility to the much-needed drug that has no true generic equivalent because of patent laws. Other companies would still be able to develop a generic substitute for insulin that the HCA could purchase and distribute at lower prices.

Other states have also considered legislation to improve access to generic drugs, with varying degrees of success. In September 2020, California Governor Gavin Newsom signed SB 852 into law, which he said would lower the costs of prescription drugs for consumers, employers, and taxpayers.

In January 2020, Newsom proposed a first-in-the-nation plan to create a state-sponsored generic drug label, and SB 852 brings the state a step closer to that goal. Under the bill, which was sponsored by Senator Richard Pan, the California Health and Human Services Agency will develop manufacturing partnerships to produce or distribute generic prescription drugs, with the goal of making medications more accessible and affordable.

“The cost of health care is way too high,” Newsom said. “Our bill will help inject competition back into the generic drug marketplace, taking pricing power away from big pharmaceutical companies and returning it to consumers.”

California officials have begun the process of identifying potential target medications and developing a strategic plan to promote state-led generic drug purchasing and manufacturing. The state has also transitioned all Medi-Cal pharmacy services from managed care to direct state payment this year, which strengthens the state’s ability to negotiate better prices with manufacturers.

These legislative shifts by the states represent a broader need for accessible and affordable medications. Individuals with chronic diseases, such as diabetes and heart disease, have an especially high need for affordable medications.

“Prescription drugs don’t work if people cannot afford to take them,” Pan said.
Fluticasone Propionate and Salmeterol Inhalation Powder
Marketed by Lannett Company, Inc

Compare to: Advair Diskus
The FDA has accepted Lannett’s abbreviated new drug application for fluticasone propionate and salmeterol inhalation powder in 3 strengths. If approved, the product would be the generic equivalent of GlaxoSmithKline’s Advair Diskus, which is indicated as a maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease and as a twice-daily treatment for asthma in patients 4 years and older. Lannett has entered into an exclusive 12-year US distribution agreement for this generic product, enabling the company to commence US distribution after FDA approval.

FOR MORE INFORMATION:
lannett.com

Lopinavir and Ritonavir Tablets
Manufactured by Camber Pharmaceuticals

Compare to: Kaletra
Camber has launched lopinavir and ritonavir tablets in 100-mg/25-mg, 60-count bottles and 200-mg/50-mg, 120-count bottles. The drug is indicated in combination with other HIV medications to control infection, prolong life, and slow disease progress. The once-daily dosing is available for both treated and treatment naive and has been shown to be as effective as twice-daily dosing in patients treated with antiviral medications. Serious adverse effects can include changes to the heart rhythm and electrical activity of the heart, interactions with other medications, liver problems, and pancreatitis.

FOR MORE INFORMATION:
camberpharma.com

VERTICALLY INTEGRATED
Emtricitabine and Tenofovir Disoproxil Fumarate Tablets
Manufactured by Lupin Limited

Compare to: Truvada
The FDA has approved Lupin’s abbreviated new drug application for emtricitabine and tenofovir disoproxil fumarate tablets in a dosage strength of 200 mg/300 mg. The medication is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection and for preexposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection. Common adverse effects can include depression, diarrhea, dizziness, nausea, stomach pain, and vomiting.

FOR MORE INFORMATION:
lupin.com

Osimertinib Tablets
Manufactured by Zydus Cadila

Compare to: Tagrisso
Zydus Cadila has received tentative FDA approval to market osimertinib tablets in dosage strengths of 40 mg and 80 mg. The product is indicated to treat lung cancer and is a kinase inhibitor. It works by slowing or stopping the growth of cancer cells by binding to specific mutated forms of the EGFR protein in some tumors. Serious adverse effects can include eye problems, heart problems including heart failure, inflammation of blood vessels in the skin, lung problems, and skin problems.

FOR MORE INFORMATION:
zyduscadila.com
Failure to Conduct DUR Is Basis for Negligence Suit

Expectations for Pharmacists Related to Drug Utilization Reviews Lead to Examination of Woman’s Death

By JOSEPH L. FINK III, JD, DSC (HON), FAPHA, BSPHARM

ISSUE OF THE CASE
DO THE PROVISIONS IN THE Omnibus Budget Reconciliation Act of 1990 (OBRA ’90) regarding drug utilization review (DUR) by pharmacists create a basis for a lawsuit when damages result from the review not having been done?

What are the legal expectations for a pharmacist regarding DURs?

FACTS OF THE CASE
A pharmacist at a chain pharmacy in a Southern state dispensed amitriptyline to a young woman. Nineteen days later, a pharmacist at the same pharmacy prepared a morphine prescription for that same patient. It was picked up 2 days after that. Six days later, the patient died from an alleged fatal adverse interaction between the 2 medications she was prescribed.

The deceased woman’s mother filed a lawsuit against the pharmacy. The lawsuit alleged that the pharmacy knew or should have known that the 2 medications could be fatal when mixed. The lawsuit also alleged that, based on that knowledge, the pharmacy staff members had a legal duty to do the following but failed to do so: call the prescriber to inquire about the appropriateness of prescribing amitriptyline and morphine simultaneously, create and follow guidelines to ensure that prescriptions do not have adverse reactions to each other, disclose material facts about the prescription, monitor the patient’s drug history, refuse to dispense the morphine after dispensing the amitriptyline, and warn about the possible adverse effects of mixing the 2 medications. The plaintiff alleged that all these obligations arose from enactment of provisions in OBRA ’90.

The pharmacy chain made a motion with the US district court where the case was being handled to dismiss the lawsuit for failure to state a legally cognizable claim. Attorneys for the chain argued that the pharmacy “had no statutory or common law duty to monitor the patient’s prescriptions or prevent her from combining adverse medications.”

THE RULING
The court ruled there was indeed a legal duty created by a state statute to monitor medication use for potential drug-drug interactions.
THE COURT’S REASONING
The court split the motion in two, focusing first on whether there was a statutory basis for these expectations in OBRA ’90 before looking at other common or statutory law origins as possible sources of the requirements.

The conclusion reached by the judge in the case was that the wording of the federal statute “did not require the defendants to review the deceased's drug profile” as was asserted.

Rather, the wording of the OBRA ’90 legislation dictated that states were required “to adopt expanded standards of pharmaceutical care for Medicaid patients as a condition on receipt of federal Medicaid funds.”

The court viewed the wording in the federal statute as “guidance to states, not private actors, on how to comply with OBRA’s mandate.”

The judge concluded that “OBRA ’90 does not create a private right of action through which [the] plaintiff could assert her claims.”

As a result, the claims based on violation of OBRA ’90 provisions were dismissed with prejudice, meaning permanently.

The attorneys for the pharmacy chain had argued that the pharmacy owed the patient “no duty whatsoever under the law of the state to review her drug profile, warn of adverse effects, or refrain from filling her prescriptions because those duties rest with the prescribing physician.”

However, the court reviewed relevant provisions in state regulations and statute, and said: “A pharmacist shall review the patient record and each prescription drug order presented for dispensing for the purpose of promoting therapeutic appropriateness by identifying…drug-drug interactions....

The lawsuit alleged that the pharmacy knew or should have known that the 2 medications could be fatal when mixed.

Upon recognizing any of the above situations, the pharmacist shall take appropriate steps to avoid or resolve the situation or problem, which shall, if necessary, include consultation with the prescribing practitioner.”

This led the judge to conclude that “although [the chain’s] pharmacists may not have had a duty to the patient under the common law of the state, the court finds that the legislature clearly imposed a statutory duty on pharmacists under particular circumstances, specifically including the duty to monitor potential drug-drug interactions.”

The pharmacy chain’s attorneys also cited an earlier case from the state dealing with what the court described as the “narrow issue of a pharmacist’s duty to warn of a drug’s potential [adverse] effects.”

However, the judge distinguished that court ruling from this case because it focused on adverse effects and not drug-drug interactions, so that argument was rebuffed.

The outcome was that the defensive arguments advanced on behalf of the pharmacy chain that were rooted in the wording of the federal OBRA ’90 statute were rejected, so that basis for the lawsuit could not be used by the plaintiff.

On the other hand, the wording of state-level regulations and statutes did provide a clear basis for the lawsuit to proceed. Accordingly, the court denied the pharmacy chain’s motion to dismiss the suit.
Telehealth Proves of Great Value During COVID-19
But State-to-State Communications and Inconsistencies Related to Licensing Present Legal Issues

By ELIZABETH H. BERNAUER AND JOSEPH L. FINK III, JD, DSC (HON), FAPHA, BSPHARM

TELEHEALTH HAS BECOME THE “it factor” when it comes to communication between health care professionals and patients, especially during the COVID-19 pandemic.

“Health care providers can provide telehealth services across state lines during the COVID-19 emergency regardless of state and local prohibitions,” the US Department of Health & Human Services (HHS) has stated.¹ This action is an attempt to counteract barriers created by the pandemic and, of course, help patients get the care they need during this time. The idea behind this expansion in telehealth is to “ease access and expand the range of services paid for through insurance,” according to HHS.² HHS issued this interpretation or ruling because of a traditional legal barrier to the use of services delivered via telehealth. The predominant legal rule traditionally has been that the provider must be licensed to practice in the state where the patient is located. That is not a challenge when the patient and provider are in the same state, but it served as a substantial hurdle for consulting with specialists. The HHS ruling eliminated that challenge.

Telehealth encompasses a wide variety of concepts, from legislation to the structure of the system, and is very complex in its manner, practice, and implementation. Legislation plays a complicated role in telehealth and is typically viewed as a barrier to diffusion.³ It has a role in state-to-state access and understanding, as well as the guidelines and standards that go with telehealth. As the use of telehealth becomes more popular, the need to understand legal and regulatory approaches grows more critical.

A few years ago, the FDA collaborated with the HHS Office of the National Coordinator for Health Information Technology to develop “strategy and recommendations on an appropriate, risk-based regulatory framework pertaining to health information technology, including mobile medical apps, that promotes innovation, protects patient safety, and avoids regulatory duplication.”⁴ A main concern is, of course, confidentiality of patient information, which would be held within a mobile application or website. The initiative attempted to address this by using passwords, special identifiers, and even secure forms of communication between patients and providers. However, this can be even more difficult to control and track when there are conflicting state regulations regarding telehealth activities.

On the federal level, “the government is investigating the expansion of telehealth to address access as well as quality and cost of care,” according to a recent article in Pharmacy and Therapeutics.⁵ Telehealth was initially directed at serving individuals with chronic conditions, but it has now become a matter of general access to ensure patients are seen appropriately. Recently, legislation was reintroduced, such as the Creating Opportunities Now for Necessary and Effective Care Technologies for Health Act and the Telehealth Innovation and Improvement Act.¹ Overall, these bills strive to enhance the quality of care for remote patients.

AUTHOR BIOS
ELIZABETH H. BERNAUER is a PharmD candidate at the University of Kentucky College of Pharmacy in Lexington.

JOSEPH L. FINK III, JD, DSC (HON), FAPHA, BSPHARM, is a professor of pharmacy law and policy and the Kentucky Pharmacists Association Professor of Leadership at the University of Kentucky College of Pharmacy in Lexington.
CHALLENGES WITH TELEHEALTH ARE NUMEROUS

"Licensing for telehealth remains a multilayered effort with state-by-state inconsistencies that have restricted the wide application of telemedicine or telepharmacy. Standard legal and/or regulatory frameworks remain elusive. Reimbursement typically follows a clear legal framework using strategies to support appropriate use of telehealth in delivering care. The lack of clarity in the law creates inconsistent reimbursement by payers to care providers. Ultimately, a clear legal framework is required if reimbursement dilemmas are to be solved," wrote Marcoux et al in the *Pharmacy and Therapeutics* article.³

It seems that telehealth and telepharmacy will be long-lasting programs that increase access to health care for all.

A widespread implementation will hopefully lead to "enhancing patient experience, improving population health, reducing costs, and improving the work life of health care providers," according to an article in the *Journal of the American Medical Informatics Association*.⁴

The largest barrier appears to be regulation across state lines. It is possible for health care providers to provide telehealth services across state lines, although that is not always the case.

Telehealth will need further regulation to maintain the momentum.

Debate has been going on for years regarding whether this sort of legislation should be put in place and what must be done to ensure patient care and the safety and security of information.

CONCLUSION

Telehealth continues to evolve and pose issues. Leaders in the field are working to get telehealth regulated in a way that is easy to view and accessible across all regions. The legislative background and regulations are changing as the environment of health care changes. Overall, telehealth is a very helpful and practical tool, but some of its aspects need tweaking to ensure safe, secure access. ■

REFERENCES


The Smarter Solution to Your Pinworm Problems

Reliable treatment at a fraction of the cost
Up to 95% savings in comparison to Rx
Rebate available on our website
Contains pyrantel pamoate
The only OTC anthelmintic recognized by the FDA
Readily available for quick & easy treatment
Sold online, at retailers nationwide, independent pharmacies & all drug wholesalers
A trusted formula since 1986
Safe & effective

ReesesPinworm.com
Reese Pharmaceutical Company
1-800-321-7178
**DIGOXIN (LANOXIN)** has a fascinating history.

*Digitalis* is a genus of 20 species of flowers that grow wild in large parts of the Eastern Hemisphere and are widely planted by gardeners in the United States. Several species have been used medically for centuries, and are still the source for digoxin, which is used to treat cardiac arrhythmia. William Withering, author of *An Account of the Foxglove and Some of Its Medical Uses With Practical Remarks on Dropsy and Other Diseases*, which was published in 1785, popularized the medical use of digitalis.

Digitalis means finger-like and refers to the flowers on the foxglove (*Digitalis purpurea*). The plant has serrated edges, tall spikes, wide leaves, and long, bell-shaped purple flowers.

Withering had the idea of gathering the leaves when the blossoms came out. The leaves were dried, either in the sun or on a pan over a fire, becoming a green powder, which was used directly or made into an infusion.

Now the leaves are extracted to yield digoxin, which is a cardiac glycoside. Digoxin inhibits the sodium ion/potassium (Na+/K+) ATPase pump in cardiac muscle cells and leads to excess intracellular Na+, indirectly leading to an increase in calcium ions in the sarcoplasmic reticulum. These increased calcium levels lead to a more forceful contraction of cardiac muscle and allow the heart to work more efficiently.

Withering used digitalis for many ailments, including edema, epilepsy, hydrothorax (fluid in the pleural cavities), ovarian cysts, and tuberculosis. He occasionally used digitalis as a treatment of last resort: “...whilst I was less expert in the management of the Digitalis, I seldom prescribed it, but when the failure of every other method compelled me to do it...if the properties of that plant had not been discovered, by far the greatest part of these patients would have died.”

Digitalis can be extremely toxic. In large and repeated doses it may cause cold sweats, disturbed vision, slow pulse, unconsciousness, and even death. Digoxin toxicity can occur during long-term therapy as well, not only after an overdose. In fact, chronic toxicity is more common than acute intoxication. Toxicity can occur even when the serum digoxin concentration is within the normal therapeutic range. Digoxin toxicity may cause anorexia, nausea, neurological symptoms, and vomiting, and can trigger fatal arrhythmias.

Visual disturbances include a tipping of the color scale toward yellow (xanthopsia), and halos around bright light. These effects can be seen in some of Vincent van Gogh's later work, his “yellow period.” Halos around the stars and moon can be seen in his painting “Starry Night” and other works. Theories suggest these effects are because of his use of foxglove for treatment of epilepsy. However, similar effects may be caused by alkaloids in *Artemisia absinthium*, which is used to brew absinthe, one of van Gogh’s preferred drinks.

On the darker side, Charles Edmund Cullen, a nurse and the most prolific serial killer in New Jersey’s history, used digoxin as his poison of choice. He was arrested in 2003 after a 16-year murder spree. Cullen reported killing at least 40 patients, but evidence suggests that he may be responsible for hundreds of deaths.
Corner Drug Is a Thriving Multigenerational Family Business

Third-Oldest Drugstore in California Celebrates a Rich History and Uses the Latest Technology to Care for Valued Patients

By KAREN BERGER, PHARMD

Corner Drug Co in Woodland, California, is a multigenerational family business and the third-oldest pharmacy in the state. Sara Shelley, PharmD, is the pharmacy’s manager and co-owner. Her grandfather, Karl Hanke, started with the company as a delivery boy in the 1940s and later became a pharmacist and owner. Karl’s daughter, Lisa Shelley, RPh, followed in his footsteps, also becoming a pharmacist and owner. Lisa’s husband, Ed, known as the pharmacy’s prankster, was the front-end manager for many years. Sara is their daughter.

Sara’s husband, Erik Daniells, is a co-owner and pharmacy technician at Corner Drug. “We have a 2-year-old daughter, Iris, whom we refer to as our ‘junior intern.’ That’s the fourth generation,” said Daniells.

That family atmosphere extends into customer service. Corner Drug provides many services to its valued patients. For example, the delivery service has been offered for 80 years and was initially done on bicycles. The pharmacy, which has solar panels on its building, is now considering shifting its delivery fleet to electric cars to lessen the impact on the environment.

Pairing cutting-edge technology with compassionate patient care is key to operating Corner Drug. The pharmacy uses several automated systems, including an Eyecon, ScriptPro, and SynMed. The staff uses PioneerRx pharmacy software, with an application for patients to communicate with employees and request refills via a secure chat service. Corner Drug also fills prescriptions throughout the county for mental health injectables and offers convenient tools such as bubble packs and MedSync.

As one of the early stores to offer Melissa & Doug products, Corner Drug offers a toy section and complimentary gift wrapping all year. During the holiday season, Santa comes to visit. The pharmacy also offers live music during the town’s First Friday art walk.
Daniells wants Corner Drug’s patients to know “that when you support a local business, you are investing in your town. We often donate to local charities, love supporting our local arts organizations and museums, and strive to make our community a better place,” he said.

“Our patients come to see us because they know we offer personalized service that can be so rare nowadays,” Daniells added. “We’re incredibly fortunate to have customers that have been loyal to us for decades.”

Corner Drug strongly believes in taking care of employees, offering “very competitive pay with robust benefits like our 401(k), health insurance, and vision insurance,” Daniells said. “We have also offered benefits like profit sharing, student loan repayment assistance, and bonuses through this pandemic. We also know that job advancement is important and have trained and sponsored several clerks to become pharmacy techs.”

Corner Drug also organizes company outings, such as group trips to local theater performances and private movie screenings. During the COVID-19 pandemic, the pharmacy employed several actors and performers who needed jobs. We also know that job advancement is important and have trained and sponsored several clerks to become pharmacy techs.”

Corner Drug also organizes company outings, such as group trips to local theater performances and private movie screenings. During the COVID-19 pandemic, the pharmacy employed several actors and performers who needed jobs.

“We love supporting their work as they start to venture back out into the community,” Daniells said.

Corner Drug has been supporting the community since 1897. (Its building was constructed in 1890 and originally housed a dry goods business until 1895.) Because of the pharmacy’s long history, pharmacy staff members have accumulated many vintage pharmacy products through the years.

“We set up a minimuseum in the front of our store,” Daniells said. “What a lot of people don’t know is that we have shelves...full of old bottles in our basement that we’ll never have room to display.”

Upstairs, however, is another story. “Many swear that our upstairs is haunted, and there have been several paranormal investigations on the site. Our building has also been featured in a web series, podcasts, and articles about the rumored hauntings,” Daniells said. “For the record, I haven’t had any ghostly encounters, but we also don’t go upstairs after dark.”

In their free time, Sara and Daniells keep busy with their 2-year-old daughter and also enjoy concerts and the theater. Daniells has an extensive background in the arts, having spent many years working around the United States as a theater conductor and pianist. His career highlight was serving as the on-screen pianist and vocal director pianist for the film Lady Bird.

The couple also has a passion for real estate. They recently purchased and are renovating a home built in 1963. They plan to move into the house this year.

“We are very fortunate to live in such a wonderful community here in northern California surrounded by friends and family,” Daniells said.
OVER THE PAST 20 YEARS, the expectations and roles of pharmacy staff members have changed drastically to meet the ever-changing demands of health care.

Pharmacists have taken on a greater role providing direct patient care as clinicians, resulting in greater reliance on pharmacy technicians. Among the many areas traditionally overseen by pharmacists where technicians have assumed responsibility, medication storage may be one of the most important. Medication storage is a vital element in pharmacy operations that affects many areas, from clinical practice to regulatory compliance. Improper storage of medications can result in a decrease in drug efficacy and may also lead to medication errors.

According to the World Health Organization, "Unsafe medication practices and medication errors are a leading cause of injury and avoidable harm in health care systems across the world," and because pharmacies are usually the last stop in the drug supply chain, technicians play an essential role in ensuring medication quality, from procurement through dispensation to patients.1

There is more to medication storage than meets the eye. Too often, the detail and effort that technicians put into complying with medication storage requirements are overlooked. Technicians are expected to understand proper medication handling, monitoring, and storage requirements, and without their expertise, pharmacies would lack crucial knowledge. Technicians face many challenges when storing medications, including environmental factors, hazardous material handling, identifying high-alert medications, legal requirements, location limitations, and specific manufacturer precautions. Without the commitment and dedication that technicians put into every aspect of their job, otherwise avoidable incidents might occur.

“One of the most easily overlooked factors that can directly impact the quality of a drug product is the condition in which medications are stored,” wrote Dantuma et al in a recent article in Pharmacy Purchasing & Products.2

Not all medications are stored in the same manner, and environmental conditions, such as light, moisture, and temperature affect drug quality. Storage temperatures vary from medication to medication and range from room temperature to subzero temperatures. Humidity, light, and moisture can accelerate product degradation and affect a medication’s stability. Generally, proper identification and management of storage requirements will result in appropriate pharmacy practices. However, pharmacies face many challenges every day, and technicians must be prepared to tackle any crisis to ensure medication integrity and mitigate any potential medication loss. Not only do environmental conditions affect proper medication storage, but specific storage requirements can create challenges as well.

With the continued development of medications and new vaccines, pharmacies face storage issues every day. The COVID-19 pandemic has created many challenges for pharmacies, but the biggest hurdle technicians have faced is the specific storage requirements for these new vac-
cines. Not only are there stringent guidelines that must be followed, but each vaccine has its own specific requirements. This places an emphasis on both proper storage and being knowledgeable about proper storage.

With Pfizer Inc the first to get emergency approval for its vaccine, demand was extremely high. Pharmacies not only faced the challenge of obtaining the vaccine, but also complying with its storage requirements. With a new vaccine of such importance, maintaining its integrity is paramount. Technicians must ensure that vaccines are stored in subzero temperatures and that there are minimal interruptions in the cold chain from procurement to administration. They are required to document and monitor every dose that enters and leaves the pharmacy.

Every day, technicians must keep these medications secure, upholding their integrity and managing any issues that may result in improper storage. The biggest hurdle created by the Pfizer vaccine is the extremely low temperature at which it must be stored. With many pharmacies lacking the subzero freezers necessary to store the vaccines, reusable shipping containers were offered as a solution. Although this allowed for more pharmacies to obtain the vaccine, it created additional responsibilities—and monitoring that fell on technicians.

Technicians are expected to be aware of, and follow, the different guidelines for each vaccine. The approval of the Moderna vaccine allowed for greater distribution while having less stringent storage conditions. Like Pfizer, the Moderna vaccine must be stored frozen until use. However, it does not require subzero temperatures. Vaccines vary when it comes to stability, whether for long-term storage, thawing for administration, or after it has been brought to room temperature.

For all vaccines, timing is critical—from preserving the cold chain when replacing dry ice in reusable containers to documenting beyond-use dating and timing for those brought to room temperature. The efficacy of the vaccine is dependent on the allotted time set by the manufacturer. Timing may seem like a minuscule detail, but when pharmacies started receiving vaccines, they were sent the vaccines that were available, resulting in shipments containing multiple manufacturers. Even though this practice provided greater public accessibility to the vaccine, it created additional responsibility and stress for pharmacy staff members. With so many critical standards for each vaccine and variables among these standards, technicians must be detailed and precise when it comes to proper storage and monitoring.

The added stresses of the pandemic, coupled with the shortage of vaccines, made proper storage even more critical. If vaccines were compromised because of a break in the cold chain or inaccurate storage, individuals’ lives could be affected. Without technicians stepping in and taking responsibility for assuring that proper precautions were followed from procurement through administration, thousands of vital doses could have been lost. Technicians are, undoubtedly, a key factor in many of the day-to-day operations within pharmacies, especially when it comes to storage, to maintain the integrity and safety of medications.

REFERENCES

The National Healthcareer Association (NHA) is honored to partner with Pharmacy Times® to educate and to advocate for pharmacy technicians. To learn more about NHA’s resources for techs, visit https://info.nhanow.com/onepartner.
Managing Medications at School Is More Than a Family Affair
Pharmacists Can Step Up Counseling and Advocate for Best Practices for Children With Chronic Illnesses

By ALEXANDRA BIENIEK

RESULTS FROM AN AMERICAN PSYCHOLOGICAL ASSOCIATION survey show that teenagers feel more stress than adults during the school year.

Life becomes even more complicated for the estimated 27% of children with chronic health conditions because constant vigilance about their health creates additional challenges. The effects of chronic illness can range from minimally to severely limiting. Some children may require frequent doctor visits or hospitalizations, affecting academic performance, school attendance, and mental health.

Approximately 20% of children take at least one prescription medication. The responsibility falls to guardians or parents to administer these treatments. But in school, they are not present to manage children's medications. Medication administration in school is a complex issue, involving many challenges and special considerations.

Adults can be forgetful, and some do not possess the medical knowledge to understand children's illnesses. How can we expect children to assume this responsibility in school?

GUIDELINES FOR MEDICATION ADMINISTRATION

Federal law requires schools receiving government funds to make accommodations for students with disabilities. However, the law is fuzzy about medication administration in schools. Some states have created standards for school districts, but the final responsibility belongs to school boards.

In September 2003, the American Academy of Pediatrics (AAP) released a resource to guide school districts when creating policies and procedures. TABLE 1 summarizes the AAP's recommendations.

CHILDREN, MEDICATION, AND SCHOOL

TABLE 2 highlights common pediatric chronic illnesses and treatments. Medication nonadherence at school may cause serious consequences. The child may feel too ill to participate, not be able to focus, or even require an emergency department visit. Hospitalizations may increase costs for the family and health care system. Other consequences include pharmacological interactions, therapy failure, or toxicity.

The World Health Organization reports that just 58% of children are adherent to medications for chronic illnesses. Ensuring pediatric medication adherence and well-being requires identifying barriers to medication administration in school. These barriers include a lack of the following: full-time school nurses or trained health care professionals, medication supply from patients, and stock emergency medications such as bronchodilator inhalers, epinephrine, and naloxone.

Health care professionals, parents, and school administrators have limited control over the school's budget and finances. Consequently, these barriers may be difficult to overcome.

However, parents and providers may advocate for schools to establish specific policies or stock emergency medications, rather than requiring

AUTHOR BIO

ALEXANDRA BIENIEK is a PharmD candidate at the University of Connecticut School of Pharmacy in Storrs.
students to have their own. Laws allow students to possess anaphylactic medications, but stock epinephrine auto-injectors are lifesaving for those who experience allergic reactions with no previous history. Despite limited resources, school administrators can seek alternative methods of improving medication administration procedures. Pharmacist involvement in schools is minimal, but they can still be valuable resources for children, parents, and the school system.

**PHARMACY IN THE SCHOOL SYSTEM**

With or without health insurance, 40% of patients report struggling to afford medications. In these situations, pharmacists can potentially alleviate medication cost using insurance resources or referrals to manufacturer assistance programs. Furthermore, pharmacists can work with primary care physicians to find alternatives or simpler regimens that may even avoid medication administration at school.

Additionally, patient counseling correlates positively with decreased administration errors and better outcomes. Patient counseling rarely includes the child, but pharmacists should educate parents and children, as soon as they are able to understand basic information, which can be as early as age 7 years.

Allowing children to self-administer medications teaches autonomy and independence. Pharmacists should emphasize dosing frequency, drug names, and proper administration techniques to encourage self-sufficiency. Common medications that children can and should self-administer include asthma medications and insulin.

**CONCLUSION**

Medication administration in schools is a complex issue. However, with proper education, planning, and procedures, children with chronic conditions can avoid serious complications, learn to successfully manage their health, and thrive in school.

---

**TABLE 1. Guidelines for Administrators and Health Personnel in Schools and School Districts**

1. Require parents and physicians to provide a written statement that includes:
   - Drug name
   - Approximate administration time
   - Diagnosis/reason for medication
   - Dose
2. Ensure medication administration policies protect student confidentiality.
3. Establish trained designee or school principal to administer medications if trained medical professional is unavailable.
4. Allow older and responsible students to self-medicate at school if appropriate.
5. Require doctor’s note for any herbal or nonprescription medications.
6. Convey to parents their responsibility to provide medications in labeled containers and other medical devices.
7. Establish protocols for documenting administration and potential errors.

---

**TABLE 2. Common Pediatric Chronic Illnesses and Treatments**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Medication(s)</th>
</tr>
</thead>
</table>
| Attention-deficit/hyperactivity disorder | • Atomoxetine (Strattera)  
|                                    | • Dextroamphetamine (Dexedrine)  
|                                    | • Guanfacine ER (Intuniv)  
|                                    | • Methylphenidate (Ritalin)                                                   |
| Asthma                             | • Albuterol sulfate (ProAir HFA)  
|                                    | • Budesonide/formoterol (Symbicort)  
|                                    | • Fluticasone propionate aerosol (Flovent HFA)  
|                                    | • Fluticasone propionate DPI inhalation powder (Flovent Diskus)             |
| Diabetes                           | • Insulin glargine (Lantus)  
|                                    | • Insulin lispro (Humalog)  
|                                    | • Liraglutide (Victoza)  
|                                    | • Metformin (Glucophage)  |
| Epilepsy                           | • Lamotrigine (Lamictal)  
|                                    | • Levetiracetam (Keppra)  
|                                    | • Oxcarbazepine (Trileptal)  
|                                    | • Sodium valproate (Depakote)  
|                                    | • Topiramate (Topamax)  |

---

For references, go to pharmacytimes.com/publications.
International Overdose Awareness Day Is Somber Reminder

Pharmacists Carry a Unique Responsibility in the Battle That Has Claimed 500,000 Lives in the Past 2 Decades

By CHRISTOPHER EPPS

INTERNATIONAL OVERDOSE AWARENESS DAY IS August 31 each year. This somber day functions as a remembrance of more than 500,000 lives lost and a reminder of how far we have come in combating addiction across America. True awareness requires reflection on the crisis’ origins, actions to mitigate its consequences, and ideas to move us forward to overcome this opioid pandemic.

THE BEGINNINGS
Several factors initiated the opioid pandemic and propelled its growth. The American Pain Society introduced pain as the fifth vital sign in 1995. That same year, Purdue Pharma marketed oxycodone (OxyContin), employing marketing campaigns that emphasized the benefits that extended pain relief provided while downplaying the implications. Purdue, as well as Allergan, Endo International, and Teva Pharmaceutical Industries Ltd, also downplayed the serious risk and likelihood of addiction that occurs with their opioids.

Fast-forward 17 years, and prescribers had written more than 259 million opioid prescriptions, enough for every adult in the country to have a bottle of pills.

Advertising and false information regarding extended-release opioids’ addictive properties are not the only reasons this epidemic continued to spiral. The FDA found that several major drug distributors were complicit in the unregulated narcotics distribution. Distributors shipped a staggering number of shipments to retail pharmacies across the country, neither questioning nor reporting them to the Drug Enforcement Administration.

Some tactics include providing seminars on pain management and safety, self-policing opioid orders without oversight, and using workarounds to evade hard limits on purchasing.

MITIGATION THAT WORKS
The United States has enacted legislation and constructed evidence-based guidelines over the past 5 years to mitigate excessive opioid use. The CDC issued evidence-based guidelines in 2016 for prescribing opioids for chronic pain in adults. The recommendations include prescribing the lowest effective dose and analyzing risks and benefits when prescribing up to 50 morphine milligram equivalents (MME) per day. Prescribers should avoid or justify daily doses of 90 MME or more. The Centers for Medicare & Medicaid Services followed in the CDC’s footsteps in 2018; Medicare Part D sponsors must limit opioid prescriptions to 7 days in opioid-naive patients.

Stricter regulations on opioids have provided mixed outcomes. Approximately 80% of new heroin users reported that prescription pills were their gateway. Individuals suffering from opioid use disorder have drug-seeking behaviors that cannot be corrected through law.

When obtaining a prescription becomes too difficult, their next step is finding illicit drugs.

The FIGURE summarizes the FDA’s actions pertaining to the opioid crisis over the past 20 years.
Pharmacists carry a unique responsibility in the fight against opioid abuse. Pharmacists in community settings are the final gatekeepers to ensure that opioid prescriptions are legitimate, employed in accordance with guidelines, and dispensed according to the law. Pharmacist-provided patient counseling and education, especially for opioid-naive patients, can make all the difference. The first step to combatting the opioid crisis is being aware of the issue and spreading knowledge about it. Public awareness has significantly increased over the past five years. Just six states had laws that expanded access to naloxone or limited criminal liability prior to two. By the end of two, four states and the District of Columbia enacted laws that provide protection for laypeople or first responders who administer naloxone.

In addition, four states now have statutes that allow pharmacists to dispense naloxone to third parties or first responders via direct prescription or standing order. The FDA approved the nasal spray formulation of naloxone for use in the community setting without medical training being required in April two. This FDA approval takes an all-hands-on-deck approach, with statistical models suggesting that one% of opioid overdose deaths can be averted.

GRIM SILVER LININGS
Although preventable overdose-related deaths still occur daily, not all lives lost are in vain. The TABLE lists the unexpected benefits evolving from the opioid crisis.

CONCLUSION
The loss of life due to an opioid overdose does not have to be senseless. We can learn from our failures and forge forward on a path that emphasizes awareness and understanding. Let’s end the stigma surrounding addiction and provide individuals with the resources they need to recover. Open dialogue is critical. Pharmacists play a key role in combatting this scourge.
FDA Approves Ivermectin Lotion to Treat Head Lice

THE FDA HAS APPROVED ivermectin 0.5% (Sklice; Arbor Pharmaceuticals) lotion for OTC use for the treatment of head lice. Ivermectin 0.5% was initially approved in February 2012 for prescription use in patients 6 months and older.

Every year, approximately 6 million to 12 million cases of head lice occur in children aged 3 to 11 years in the United States. Head lice are most common among preschool children in childcare, elementary school children, and members of a household in which children have lice.

Ivermectin 0.5% is for external use only and should be used on dry hair or the scalp in accordance with label instructions. The lotion will be marketed as a nonprescription drug and will no longer require a prescription.

—Sara Karlovitch

Investigators Find Missing Piece to Lyme Disease Puzzle

THROUGHOUT THE COVID-19 PANDEMIC, Assistant Professor Brandon Jutras and his laboratory at Virginia Polytechnic Institute and State University in Blacksburg have been analyzing the ongoing Lyme disease epidemic and have found a possible missing factor in its spread, according to recent findings published in the journal PLOS Pathogens.

“This discovery furthers our understanding of how Borrelia burgdorferi causes inflammation and disease,” lead study author Mari Davis said in a statement. “It is a testament to how unique this bacterium is and how we need to keep working to understand more about what is going on behind the scenes in order to develop future diagnostics and treatments.”

In 2019, Jutras identified peptidoglycan, the mesh-like bag made by bacteria to protect the inside of their cell, as the likely cause of the most common late-stage Lyme disease symptoms—inflammation and Lyme arthritis.

In this newest development, his lab discovered a protein—NapA (or, neutrophil-attracting protein A)—that plays an amplifying role in causing inflammation in patients with Lyme arthritis. The immunomodulatory molecule can “recruit” immune cells, or neutrophils, toward the inflammatory peptidoglycan, according to the study authors.

The laboratory tests showed that neutrophils rapidly migrate toward the side with NapA, proving that the protein is able to give off chemical signals that attract neutrophils in the direction of it and the peptidoglycan.—Jill Murphy

Salt-Based Mosquito-Control Products Are Ineffective

THE RESULTS OF A NEW STUDY published in the Journal of Medical Entomology show that products claiming to reduce mosquito populations with salt-water solutions are not effective.

Investigators conducted a series of laboratory tests in 5 locations using 9 species of mosquito, finding no evidence that adult mosquitoes are killed by salt ingested at concentrations used in several popular mosquito-control products.

The team assembled feeding trials during which caged mosquitoes were offered 1 of 4 diets for a week: salt water only, sugar water only, water only, or a salt-and-sugar-water mixture. The concentrations in the diets were based on the product description of the most widely available salt-based mosquito-control device on the market.

“The consistency in the findings was a bit of a surprise given that nature is messy,” study coordinator Donald Yee, PhD, BCE, said in a statement. “We’d expect there to be a lot of variation in responses to the diets we offered, but broadly speaking, adding salt to plain water or sugar water didn’t lead to increased mosquito death. Adult mosquitoes just don’t die faster because they drink salt water.”

The investigators recommended that the public turn to local mosquito-control agencies for proper guidance or use traditional practices and products to reduce the risk of mosquito-borne disease.—Jill Murphy

Summer Pest Watch

By AISLNN ANTRIM

Investigators Find Missing Piece to Lyme Disease Puzzle

Throughout the COVID-19 pandemic, Assistant Professor Brandon Jutras and his laboratory at Virginia Polytechnic Institute and State University in Blacksburg have been analyzing the ongoing Lyme disease epidemic and have found a possible missing factor in its spread, according to recent findings published in the journal PLOS Pathogens.

“This discovery furthers our understanding of how Borrelia burgdorferi causes inflammation and disease,” lead study author Mari Davis said in a statement. “It is a testament to how unique this bacterium is and how we need to keep working to understand more about what is going on behind the scenes in order to develop future diagnostics and treatments.”

In 2019, Jutras identified peptidoglycan, the mesh-like bag made by bacteria to protect the inside of their cell, as the likely cause of the most common late-stage Lyme disease symptoms—inflammation and Lyme arthritis.

In this newest development, his lab discovered a protein—NapA (or, neutrophil-attracting protein A)—that plays an amplifying role in causing inflammation in patients with Lyme arthritis. The immunomodulatory molecule can “recruit” immune cells, or neutrophils, toward the inflammatory peptidoglycan, according to the study authors.

The laboratory tests showed that neutrophils rapidly migrate toward the side with NapA, proving that the protein is able to give off chemical signals that attract neutrophils in the direction of it and the peptidoglycan.—Jill Murphy

Salt-Based Mosquito-Control Products Are Ineffective

The results of a new study published in the Journal of Medical Entomology show that products claiming to reduce mosquito populations with salt-water solutions are not effective.

Investigators conducted a series of laboratory tests in 5 locations using 9 species of mosquito, finding no evidence that adult mosquitoes are killed by salt ingested at concentrations used in several popular mosquito-control products.

The team assembled feeding trials during which caged mosquitoes were offered 1 of 4 diets for a week: salt water only, sugar water only, water only, or a salt-and-sugar-water mixture. The concentrations in the diets were based on the product description of the most widely available salt-based mosquito-control device on the market.

“The consistency in the findings was a bit of a surprise given that nature is messy,” study coordinator Donald Yee, PhD, BCE, said in a statement. “We’d expect there to be a lot of variation in responses to the diets we offered, but broadly speaking, adding salt to plain water or sugar water didn’t lead to increased mosquito death. Adult mosquitoes just don’t die faster because they drink salt water.”

The investigators recommended that the public turn to local mosquito-control agencies for proper guidance or use traditional practices and products to reduce the risk of mosquito-borne disease.—Jill Murphy
**Case Studies**

**By LEANNE VARGA, LAUREN BRONSON, AND STEFANIE C. NIGRO, PHARMD, BCACP, CDCES**

**CASE 1**

AG is a 65-year-old woman who has type 2 diabetes. She recently started insulin therapy because of worsening glycemic control. AG’s antidiabetic regimen includes 5 units of insulin aspart before breakfast, 20 units of insulin glargine at bedtime, and 1000 mg of metformin twice daily. She tests 4 times per day, at bedtime and before meals. AG wonders why her blood glucose is so high every morning. Upon review of her logs, the pharmacists notice that her bedtime readings average 89 mg/dL, with subsequent fasting readings averaging more than 200 mg/dL the past week. AG does not snack late at night and says that she takes her medications as directed every day.

**What is the explanation?**

AG’s morning hyperglycemia may be the result of either the dawn phenomenon or Somogyi effect. To distinguish the cause, instruct her to test her glucose levels around 3 AM. If AG is experiencing nocturnal hypoglycemia, it is most likely the Somogyi effect; her body compensates for low sugar by secreting glucagon, causing rebound hyperglycemia in the morning. This can be the result of not eating enough carbohydrates at night or taking too much insulin. The pharmacist should assess AG’s insulin technique and verify her doses to ensure that she is using the insulin correctly. She may need a dose reduction of her insulin to improve her glucose readings. The pharmacist can recommend decreasing AG’s glargine to 16 units at bedtime.

**CASE 2**

EG is a 51-year-old woman who has been experiencing hot flashes for the past 6 months. She mentions that she has not spoken to her physician because she heard these are normal menopause symptoms. However, during the past month, the symptoms have been disrupting EG’s daily life and sleep. She smokes half a pack of cigarettes per day and has not been able to go to the gym to exercise because of COVID-19 facility restrictions. EG’s past medical history includes osteopenia, but she is otherwise healthy. EG recently spoke to a neighbor who said that she also had hot flashes and that her physician prescribed a hormone tablet, which helped. EG wonders whether this treatment could work for her as well.

**What should the pharmacist tell her?**

Vasomotor symptoms, or hot flashes, are a common symptom of menopause. Because EG’s symptoms are disrupting her life, hormonal replacement therapy (HRT), such as estrogen alone or in combination with a progestin, could be an option as long as she has not yet reached menopause. An individual’s decision to begin HRT should be for the shortest duration possible. Lifestyle changes, such as exercising regularly, maintaining a healthy body weight, and refraining from smoking, have also been shown to provide some relief from hot flashes. If HRT is not appropriate, treatment should be for the shortest duration possible. Lifestyle changes, such as exercising regularly, maintaining a healthy body weight, and refraining from smoking, have also been shown to provide some relief from hot flashes. If HRT is not appropriate, treatment should be for the shortest duration possible.

Answers

For references, go to pharmacytimes.com/publications.

**CASE 1:** AG’s morning hyperglycemia may be the result of either the dawn phenomenon or the Somogyi effect. To distinguish the cause, instruct AG to test her glucose levels around 3 AM. If AG is experiencing nocturnal hypoglycemia, it is most likely the Somogyi effect; her body compensates for low sugar by secreting glucagon, causing rebound hyperglycemia in the morning. This can be the result of not eating enough carbohydrates at night or taking too much insulin. The pharmacist should assess AG’s insulin technique and verify her doses to ensure that she is using the insulin correctly. She may need a dose reduction of her insulin to improve her glucose readings. The pharmacist can recommend decreasing AG’s glargine to 16 units at bedtime.

**CASE 2:** EG’s symptoms are disrupting her life, and she wonders whether hormonal replacement therapy could work for her as well. The pharmacist should recommend lifestyle changes, such as exercising regularly, maintaining a healthy body weight, and refraining from smoking, to provide some relief from hot flashes. If HRT is not appropriate, treatment should be for the shortest duration possible. If HRT is appropriate, the lowest effective dose of HRT should be used. EG should be screened for a history of cardiovascular and thrombotic disease, along with breast cancer. If appropriate, the lowest effective dose of HRT should be used for symptom relief. Treatment should be for the shortest duration possible.

**AUTHOR BIOS**

LEANNE VARGA and LAUREN BRONSON are PharmD candidates at the University of Connecticut School of Pharmacy in Storrs.

STEFANIE C. NIGRO, PHARMD, BCACP, CDCES, is an associate clinical professor at the University of Connecticut School of Pharmacy.
Fun Facts

Q: What were chain saws invented for in the 18th century?
A: Childbirth. After centuries of dangerous, experimental Cesarean sections, 2 Scottish doctors developed a prototype of the chain saw to use in symphysiotomies, a surgical procedure in which a joint above the vulva is severed to widen the pelvis and potentially make childbirth easier. The original design of the chain saw was based on a watch chain with teeth that moved through a hand crank, which was later mechanized in the late 19th century to increase ease of use. The invention was eventually adopted by the timber industry in 1905, allowing it to be applied to trees rather than women.

Q: What remedy saved a man from execution in the 16th century?
A: A Terra sigillata. In the 16th century, many royals lived in fear of being poisoned because poisons were easily accessible in apothecaries. In 1581, a prisoner in Germany named Wendel Thumblardt decided to use this knowledge to save his life, as he was to be imminently hanged. He had met a physician who claimed that terra sigillata, or sealed earth, worked as a panacea for almost anything but said that it was specifically helpful as an antidote to poison. Thumblardt told Prince Wolfgang II, his captor, that he would agree to be poisoned and would consume terra sigillata to test its efficacy. If the tablets did not work, then Thumblardt would die as planned, and if they did, he would win his freedom. Although the poison made him very sick, he survived, and Wolfgang II bought a lifetime supply of terra sigillata from the physician.

Q: What was thought to treat hemorrhoids in ancient Greece?
A: Fire. In the 4th century BC, Hippocrates, the founding father of medicine, thought that the best cure for hemorrhoids was through the curative properties of fire. He said that by placing a hot iron against hemorrhoids, they could be cauterized and thus cured. Following this application, Hippocrates recommended applying a poultice of lentils and vegetables to the wound to promote healing of the burn, though he said that such burns were a mere adverse effect of the panacea that was the intense heat of fire.
Individualized Care for Patients With Immune Thrombocytopenia: The Role of the Pharmacist

Overview
Immune thrombocytopenia (ITP), formerly known as immune or idiopathic thrombocytopenic purpura, is an autoimmune disorder primarily characterized by destruction and diminished production of platelets. ITP can affect both pediatric and adult patients, and phenotypically can manifest as either a transitory or chronic disease process. Although bleeding symptoms are generally the impetus for treatment, ITP is a multifactorial ailment and many patients with ITP also experience fatigue and diminished health-related quality of life (HRQOL). Several treatment modalities have historically been used to manage newly diagnosed ITP: corticosteroids, anti-D immune globulin, intravenous immune globulin (IVIG), or observation. Although bleeding symptoms are generally the impetus for treatment, ITP is a multifactorial ailment and many patients with ITP also experience fatigue and diminished health-related quality of life (HRQOL). Several treatment modalities have historically been used to manage newly diagnosed ITP: corticosteroids, anti-D immune globulin, intravenous immune globulin (IVIG), or observation. Management of persistent/chronic ITP is less scripted, and often includes a number of patient-specific interventions applied in a trial-and-error fashion, including but not limited to rituximab, thrombopoietin receptor agonists (TPO-RAs), other immunosuppressants (eg, azathioprine, cyclosporine, cyclophosphamide), spleen tyrosine kinase (SYK) inhibition, and/or splenectomy.

Several groups have issued and recently updated clinical practice guidelines outlining practice recommendations for the management for patients with ITP, and research in the field has blossomed over the past several decades with the emergence of various novel therapeutic approaches. As a disease entity, ITP is prime for patient-centered shared decision making, and with several treatment regimens approved for use in the United States, as medication experts, pharmacists are uniquely positioned to play an impactful role in the management of this patient population.

Definitions
In 2007, an international working group (IWG) standardized the terminology, definitions, and outcome criteria of pediatric...

EDUCATIONAL OBJECTIVES
At the completion of this activity, the participant will be able to:
• Examine immune thrombocytopenia (ITP) pathophysiology, clinical presentation, and impact on patient quality of life
• Analyze the latest data on the efficacy, safety, dosing, and administration of current treatment options for ITP
• Demonstrate the pharmacist’s role in the management of patients with ITP

TARGET AUDIENCE: Pharmacists
ACTIVITY TYPE: Application
RELEASE DATE: July 30, 2021
EXPIRATION DATE: September 15, 2022
ESTIMATED TIME TO COMPLETE ACTIVITY: 2.0 hours
FEE: This lesson is offered for free at www.pharmacytimes.org.
and adult ITP. These definitions remain relevant and in use to date; however, significant heterogeneity in the application of response definitions has been observed in the documented ITP literature.4

Primary versus Secondary ITP
Ultimately, ITP is considered a diagnosis of exclusion. Primary ITP occurs in the absence of known causes. Secondary ITP is incident to an underlying disease. When treated, primary ITP is often managed with immunomodulatory therapies, whereas secondary ITP is generally managed by addressing the underlying condition (eg, lymphoproliferative disorder, infection).2

Newly Diagnosed versus Persistent versus Chronic ITP
The IWG defines 3 main phases of ITP based on disease duration. Disease lasting fewer than 3 months is termed newly diagnosed, whereas disease lasting 3 to 12 months is considered persistent, and a duration over 12 months is considered chronic.2 Although the definitions follow a time-dependent progression from newly diagnosed to persistent to chronic disease, not all patients ultimately progress to persistent or chronic disease. Spontaneous remission is feasible in the first 12 months after diagnosis, especially for pediatric patients, where more than 60% of cases resolve.1 Understanding each patient’s phase of ITP is vital to weighing treatment choices and making management decisions.

Disease Severity
Unlike other hematologic disease states that define severity based on laboratory values, ITP severity is defined by the IWG by bleeding symptoms. For those cases with bleeding symptoms necessitating treatment, or breakthrough bleeding while on treatment requiring an escalation/adjustment of treatment, the term severe ITP is used.2

Response to Treatment
A response to an ITP therapy is defined by the IWG as achieving a platelet count of 30 to 99 x 10^9/L and at least a 2-fold increase from baseline platelet count in the absence of bleeding. A complete response is defined as achieving a platelet count of 100 x 10^9/L or higher in the absence of bleeding.2 Despite the IWG definitions, many clinical trials of ITP therapies have used alternative definitions, most commonly defining response as achieving or maintaining a platelet count above or equal to 50 x 10^9/L.4

Pathophysiology, Clinical Presentation, and Impact of ITP
Pathophysiology
Platelets play an essential role in the hemostatic cascade. Platelets arise from megakaryocytes, which are regulated by the megakaryopoietic hormone thrombopoietin (TPO).10 ITP is an autoimmune process resulting in premature platelet destruction, thought to be primarily driven by autoantibody production.3 Antibody-coated platelets are susceptible to destruction in the liver and/or spleen through activation of Fcγ receptors.3 SYK participates in the signaling of activated Fcγ receptors, leading to macrophage phagocytosis of antibody-coated platelets.5,10 In patients with ITP, circulating platelets only survive hours, rather than the typical lifespan of 5 to 7 days.12,13 Multiple therapeutic approaches in ITP are targeted at halting this premature destruction.

Additionally, megakaryocyte function may be impaired, resulting in diminished production of compensatory platelets and an overall platelet net loss.3 Although quantitatively deficient, individuals with ITP generally have hemostatically efficient platelets that are fresh, large, and filled with granules; this could explain why clinically severe bleeding is relatively infrequent as compared with other patients experiencing thrombocytopenia from non-ITP causes.12,13

Clinical Presentation
Most patients do not exhibit clinically relevant bleeding until the platelet count is below 20 to 30 x 10^9/L, and may even remain asymptomatic with platelets in the 10 to 20 x 10^9/L range.14 Risk factors for bleeding in patients with ITP include concomitant use of anticoagulant/antiplatelet therapies or nonsteroidal anti-inflammatories, age over 65 years, female sex, and platelet count below 10 x 10^9/L.3,15 Patient presentation is variable, ranging from an asymptomatic incidental laboratory finding of platelet count below 100 x 10^9/L to frank mucosal bleeding.14 Unlike patients with severe factor deficiencies (eg, hemophilia), patients with ITP rarely present with significant musculoskeletal bleeds.14 In a cross-sectional study of adult patients with newly diagnosed ITP in France, at diagnosis, 6.6% of patients presented with severe bleeding (eg, intracranial hemorrhage, hematuria, gastrointestinal hemorrhage), 30% with mucosal bleeding, and 58% with any bleeding symptoms.15 Pediatric patients tend to present with acute-onset, diffuse petechiae and bruising, oftentimes preceded by recent viral infection.15 Although most children present with cutaneous manifestations, fewer than one-third of pediatric patients will present with overt bleeding.13
Impact of ITP

ITP can pose a significant burden on patient HRQOL, often impacting treatment decisions. In addition to the classic hematologic sequelae of thrombocytopenia, ITP has been associated with fatigue, depression, anxiety, and overall diminished HRQOL.5,6 Fatigue is frequently cited as the most common non-hematologic symptom in patients with ITP, reported in 20% to 50% of adults and, although difficult to quantify in pediatrics, one pediatric study reported an incidence of 50% to 60%.1,6 Interestingly, fatigue may not necessarily correspond with degree of thrombocytopenia, and improving the platelet count may not always ameliorate the fatigue.16

In the cross-sectional I-WISh survey of 1507 adult patients with ITP, 75% or more patient respondents reported diminished ability to perform daily tasks, capacity to exercise, and energy levels.5 In the same study, nearly half reported a substantial impact on emotional well-being and also had either reduced or seriously considered reducing working hours.17 Quality-of-life disturbance is not unique to adult patients; in a prospective cohort of 120 pediatric patients with ITP, quality of life was the most cited reason for starting second-line treatments for ITP.18

Treatment Landscape

Along with splenectomy, medical therapy with corticosteroids, IVIG, anti-D immune globulin, and nonspecific immunosuppressants have been the cornerstone of ITP treatment for decades.19 Several novel therapies for ITP emerged in the 2000s, including TPO-RAs eltrombopag, romiplostim, and avatrombopag, and the first-in-class SYK inhibitor fostamatinib.7

Treatment of Pediatric Patients

Newly Diagnosed ITP

Given that many children experience disease remission, observation, or a “watch and wait policy” is an acceptable treatment modality for most pediatric patients with ITP, regardless of platelet count. The decision to watch or treat pediatric patients should be made jointly with the patient/caregiver and weigh several considerations, including activity level (eg, does the child play contact sports?), access to emergency care, recent trauma (especially head), and potential reasonable rationale to avoid certain agents.1,7,8

In patients without life-threatening bleeding requiring treatment, outpatient management is generally preferred over hospitalization. Short-course corticosteroids (eg, prednisone), anti-D immune globulin, and IVIG are all suggested front-line options. The American Society of Hematology (ASH) guidelines preferentially suggest corticosteroids over anti-D immune globulin or IVIG in patients with non–life-threatening mucosal bleeds and/or reduced HRQOL.1

When corticosteroids are administered, the ASH guidelines recommend courses of 7 days or fewer, and suggest prednisolone (2-4 mg/kg/day, max 120 mg per day for 5-7 days) over dexamethasone (0.6 mg/kg/day, max 40 mg per day for 4 days).1 The international consensus report (ICR) recommends prednisolone at a dose of 4 mg/kg/day, max 200 mg/day for 4 days or 1 to 2 mg/kg/day, max 80 mg/day for 1 to 2 weeks.7 Onset of action for corticosteroids is generally observed within 1 to 2 weeks of administration.3,8

Responses to anti-D immune globulin or IVIG are generally observed within 1 to 3 days after administration.5,3,8 Dosing of IVIG is typically a single dose of 0.8 to 1 gram/kg, which can be repeated if necessary.7,8 Headaches may accompany administration of IVIG, and acetaminophen can be used after administration for symptomatic control.7

Because of the mechanism of action and the potential to induce intravascular hemolysis, only patients who are Rh+, non-splenectomized, direct antiglobulin test (DAT) negative, and with adequate hemoglobin greater than or equal to 9 to 10 grams/dL are candidates for anti-D immune globulin.19 If administering intravenous anti-D immune globulin, the ICR-recommended dose is 75 mcg/kg, and premedication with a high-dose corticosteroid is recommended.3 In the event of a life- or organ-threatening bleed, high-dose platelet transfusion can be given in conjunction with high-dose IV corticosteroids (eg, methylprednisolone 30 mg/kg IV) with or without IVIG and/or anti-D immune globulin.7

Persistent/Chronic ITP

As 60% to 75% of children experience spontaneous remission within the first year of diagnosis, most pediatric patients will not progress to chronic ITP.1,7,8 Identified risk factors for development of chronic ITP in children include higher platelet count at time of diagnosis, absence of infectious prodrome, older age, and female sex.7 Second-line options for children unresponsive to the first-line treatments discussed above include the TPO-RAs, rituximab, and splenectomy. Both the ASH and ICR publications favor TPO-RAs over rituximab or splenectomy.1,7 Although rituximab can induce responses in up to 60% to 70% of patients, just 20% to 30% will maintain long-term remission.20 Conversely, splenectomy can induce lasting response in a majority of patients; however, there are long-term ramifications associated with surgical splenectomy, including the need for antibacterial prophylaxis. Splenectomy is largely considered a last resort in children with ITP.7
In the event of loss or absence of response to one TPO-RA, an alternative TPO-RA can be used, or an immunosuppressant such as mycophenolate mofetil can be added to the therapeutic regimen. Although national guidelines do not make specific recommendations for subsequent lines of therapy beyond TPO-RAs, rituximab, and splenectomy, other agents have been investigated, including thiopurines (eg, 6-mercaptopurine, azathioptine), cyclosporine, cyclophosphamide, danazol, dapsone, and vinca alkaloids (eg, vincristine, vinblastine).21

**STAR***

When considering treatment of a pediatric patient with newly diagnosed ITP, what are the advantages and disadvantages of corticosteroids? IVIG? Anti-D immune globulin?

*S = Stop; T = Think; A = Assess; R = Review

**Spotlight on TPO-RAs**

Contrary to approaches used in first-line treatment, TPO-RAs are not used to halt platelet destruction; rather, they act as megakaryopoietic stimulatory agents to enhance platelet production.10 Three TPO-RAs are commercially available in the United States: eltrombopag (Promacta), romiplostim (Nplate), and avatrombopag (Doptelet). Eltrombopag and romiplostim were first FDA approved in 2008, and avatrombopag followed in 2018.25-27 Eltrombopag and avatrombopag are orally available small molecules that bind at the transmembrane domain of the TPO receptor (also known as the c-MPL receptor) on the surface of megakaryocytes.10,28 Alternatively, romiplostim is a subcutaneous Fc-peptide fusion protein “peptibody” that has been evaluated in recent years with promising outcomes, but are not yet recommended by international guidelines.7,20,24

**Persistent/Chronic ITP**

High-quality data regarding medical management of persistent/chronic ITP in adult patients, including large randomized controlled trials, have emerged over the past several decades.16 TPO-RAs, rituximab, and splenectomy are identified by both the ASH and ICR publications as reasonable second-line therapies when ITP persists 3 months or longer.1,7 Additionally, the ICR identifies the SYK inhibitor fostamatinib, which is administered by mouth twice daily, as a potential subsequent therapy with robust evidence.7 Because of the possibility of spontaneous remission in the first year after diagnosis, splenectomy should ideally be deferred until the patient has progressed to chronic disease.1,7

Selection of second-line and later lines of therapy for adult patients with persistent or chronic ITP should prioritize patient preferences.1,7 Although not FDA approved for this indication, intravenous rituximab generally given weekly for 4 doses may be a reasonable option for those patients with persistent or chronic ITP who want to avoid potentially lifelong therapy. Similarly, splenectomy may be considered in those with chronic disease, but is not recommended until 12 months or more have elapsed.1,7 Conversely, if the patient values durable responses but wants to avoid surgery, the TPO-RAs would be ideal.7 Given the chronic nature and HRQOL implications of ITP, it is paramount to align patient preference and treatment goals.

**Treatment of Adult Patients**

Newly Diagnosed ITP

As with pediatric patients, the decision to treat and therapy selection should be tailored to the individual patient.1,7 For newly diagnosed adults with platelets equal to or above 30 x 10^9/L who are either asymptomatic or who have minor mucosal bleeding only, ASH guidelines recommend observation in lieu of treatment; for those with platelets below 30 x 10^9/L, treatment is suggested over observation.1

If treatment is pursued for an adult patient with newly diagnosed ITP, both ASH and ICR recommendations identify corticosteroids as standard first-line therapy, provided there are no contraindications to use, such as psychiatric disorders or uncontrolled diabetes.1,7 High-dose dexamethasone (40 mg daily x 4 days) and conventional prednisolone (0.5-2 mg/kg/day x 2-4 weeks) are preferred.1,7,22,23 A systematic review and meta-analysis failed to identify a significant difference in platelet response at 6 months between the 2 regimens, but is not recommended until 12 months or more have elapsed.1,7 If, however, the patient values durable responses but wants to avoid surgery, the TPO-RAs would be ideal.7 Given the chronic nature and HRQOL implications of ITP, it is paramount to align patient preference and treatment goals.

**Spotlight on TPO-RAs**

Contrary to approaches used in first-line treatment, TPO-RAs are not used to halt platelet destruction; rather, they act as megakaryopoietic stimulatory agents to enhance platelet production.10 Three TPO-RAs are commercially available in the United States: eltrombopag (Promacta), romiplostim (Nplate), and avatrombopag (Doptelet). Eltrombopag and romiplostim were first FDA approved in 2008, and avatrombopag followed in 2018.25-27 Eltrombopag and avatrombopag are orally available small molecules that bind at the transmembrane domain of the TPO receptor (also known as the c-MPL receptor) on the surface of megakaryocytes.10,28 Alternatively, romiplostim is a subcutaneous Fc-peptide fusion protein “peptibody” that
binds directly at the TPO binding site on c-MPL. 26 If refractory to a particular TPO-RA, switching to an alternative TPO-RA may be effective. 7,29 Although the TPO-RA may be continued indefinitely in patients responding to therapy, 10% to 30% of patients may experience continued responses after discontinuation of the TPO-RA. 10,30 A recent panel of ITP experts recommend slowly tapering the TPO-RA in those able to maintain platelet counts over 50 x 10^9/L for at least 6 months without concomitant therapy, provided the patient has no comorbidities and is not on concomitant anticoagulant/antiaggregate therapy. 30

Eltrombopag

Eltrombopag is FDA approved for the treatment of persistent and chronic ITP in adults and children older than 1 year. 25 Eltrombopag is commercially available in tablets of varying sizes (ie, 12.5 mg, 25 mg, 50 mg, 75 mg) and powder packets for reconstitution (ie, 12.5 mg and 25 mg), facilitating dose adjustments based on platelet response and/or AEs. Because eltrombopag is a chelating agent that binds polyvalent cations

TABLE 1. STARTING DOSE AND RESPONSE-BASED DOSE MODIFICATIONS OF THROMBOPOIETIN RECEPTOR AGONISTS IN IMMUNE THROMBOCYTOPENIA 17,26-27

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pediatric starting dose</th>
<th>Adult starting dose</th>
<th>Starting dose modifications?</th>
<th>Adjustment for platelets &lt;50 x 10^9/L</th>
<th>Adjustment for platelets 200-400 x 10^9/L</th>
<th>Adjustment for platelets &gt;400 x 10^9/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avatrombopag</td>
<td>N/A</td>
<td>20 mg by mouth daily</td>
<td>Yes; see Table 1a. Start at dose level 3 if taking moderate or strong dual inhibitors of CYP2C9 and CYP3A4. Start at dose level 6 if taking moderate or strong dual inducers of CYP2C9 and CYP3A4</td>
<td>Increase by 1 dose level (see Table 1a)</td>
<td>Decrease by 1 dose level (see Table 1a)</td>
<td>Stop until platelets &lt;150 x 10^9/L; resume with a 1 dose level reduction (see Table 1a)</td>
</tr>
<tr>
<td>Eltrombopag</td>
<td>1-5 years: 25 mg by mouth daily</td>
<td>50 mg by mouth daily</td>
<td>Yes; decrease to 25 mg by mouth daily for patients of Asian ancestry or hepatic impairment (Child-Pugh class A, B, C). If Asian ancestry and hepatic impairment, 12.5 mg by mouth daily</td>
<td>Increase by 25 mg by mouth daily until max 75 mg by mouth daily. For patients starting at 12.5 mg, increase to 25 mg first before increasing by 25 mg.</td>
<td>Decrease daily dose by 25 mg and reassess in 2 weeks. For patients on 25 mg, decrease by 12.5 mg.</td>
<td>Stop until platelets &lt;150 x 10^9/L; resume with a 25 mg reduction (or 12.5 mg, if patient was on 25 mg). Discontinue if platelets &gt;400 x 10^9/L after 2 weeks on lowest dose.</td>
</tr>
<tr>
<td>Romiplostim</td>
<td>1 mcg/kg SC weekly; either in infusion center or by self-administration. Volume should be rounded to the nearest hundredth mL.</td>
<td>None</td>
<td>Increase by 1 mcg/kg weekly</td>
<td>Reduce by 1 mcg/kg if 200-400 x 10^9/L for 2 consecutive weeks.</td>
<td>Hold until platelets &lt;200 x 10^9/L; resume with a 1 mcg/kg reduction.</td>
<td></td>
</tr>
</tbody>
</table>

SC, subcutaneous.

TABLE 1A. AVATROMBOPAG DOSE LEVELS 27

<table>
<thead>
<tr>
<th>Dose level</th>
<th>Avatrombopag dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20 mg once weekly</td>
</tr>
<tr>
<td>2</td>
<td>20 mg twice weekly or 40 mg once weekly</td>
</tr>
<tr>
<td>3</td>
<td>20 mg three times a week</td>
</tr>
<tr>
<td>4</td>
<td>Starting dose for patients not on interacting agents</td>
</tr>
<tr>
<td>5</td>
<td>20 mg once daily</td>
</tr>
<tr>
<td>6</td>
<td>20 mg x 3 days and 20 mg x 4 days, repeat sequence weekly</td>
</tr>
<tr>
<td>7</td>
<td>40 mg once daily</td>
</tr>
</tbody>
</table>

SC, subcutaneous.
(e.g., calcium, iron, magnesium), administration of medications/food that contain these cations should be separated by 2 hours before or 4 hours after eltrombopag dose. Failure to separate the interacting substance may result in a clinically meaningful reduction in the absorption of eltrombopag. Additionally, coadministration with high-fat foods significantly impacts drug pharmacokinetics, with a reduction in the maximum concentration and area under the curve. The FDA-approved starting dose and dose adjustments are outlined in Table 1. However, an alternative dosing strategy of only 2 to 4 times a week has been described in a small cohort of adults with promising responses.

The EXTEND study evaluated the long-term safety and efficacy of daily eltrombopag in 302 adults with ITP on therapy for a median of 2.4 years (range, 2 days to 8.8 years). Defining response as platelets greater than or equal to 50 x 10^9/L, 86% of patients achieved a response, with 52% sustaining a continuous response for 25 weeks or longer. Long-term therapy with eltrombopag was well tolerated. Grade 3 or less thromboembolic events occurred in 6% of patients, and hepatotoxicity was seen in 15% of those treated.

Romiplostim

Romiplostim is FDA approved for the treatment of ITP in adults and children older than 1 year. In adults, the approval is based on clinical benefit established in 2 parallel phase 3 placebo-controlled trials of patients with and without prior splenectomy. In these trials, the median romiplostim dose was 2 to 3 mcg/kg/week, and an overall platelet response was seen in 88% and 79% of those who were non-splenectomized and splenectomized, respectively. Additionally, bleeding events were similar between treatment arms and placebo. Following these 2 studies, an extension study was completed, showing continued benefit with romiplostim at a median duration of 60 weeks. Romiplostim is approved at a starting dose of 1 mcg/kg subcutaneous once a week with weekly escalations of 1 mcg/kg for inadequate response. Most adults do not exhibit a response until a median of 3 to 5 mcg/kg/week, and many pediatric patients require the maximum dose of 10 mcg/kg/week. If a patient requires rapid response, it may be reasonable to consider more aggressive dosing by either initiating therapy at a higher dose and/or escalating by more than 1 mcg/kg/week. Overall, romiplostim is well tolerated, with headache being the most common AE seen in 5% or more of patients compared with placebo, with 48% of cases being mild in severity, 31% moderate, and 21% severe.

Avatrombopag

FDA approved in 2018, avatrombopag is the most recently available small-molecule TPO-RA with initial dosing once daily, then adjusted based on platelet count. Avatrombopag lacks clinically significant drug–food interactions. Safety and efficacy of avatrombopag in adult patients with chronic ITP have been established in phase 2 and 3 placebo-controlled trials. In the phase 3 trial, median cumulative number of weeks with platelets greater than or equal to 50 x 10^9/L was 12.4 in the avatrombopag group as compared with 0 in the placebo group (P < .0001), and at day 8 of treatment, 66% of the avatrombopag group achieved platelets greater than or equal to 50 x 10^9/L, as compared with 0% in the placebo group (P < .0001). The most common AEs occurring in greater than or equal to 10% of patients with ITP included headache, epistaxis, upper respiratory tract infection, arthralgias, gingival bleeding, petechiae, and nasopharyngitis. Serious AEs occurred in 9% of patients, with the most common being headache (1.6%).

Spotlight on SYK Inhibition

The SYK inhibitor fostamatinib is given twice daily in adult patients with chronic ITP who have not adequately responded to prior therapies. Fostamatinib was FDA approved based on 2 identical randomized placebo-controlled trials in adult patients with persistent/chronic ITP: the FIT1 trial in North America, Australia, and Europe, and the FIT2 trial in Europe. Patients were initiated on 100 mg by mouth twice daily and escalated up to 150 mg twice daily if necessary, based on platelet count. Collectively, 101 patients received fostamatinib, with overall platelet responses (defined as platelets ≥50 x 10^9/L at least once in the first 12 weeks) observed in 43% of the fostamatinib arm versus 14% with placebo (P = .0006). Stable platelet responses, defined as platelets greater than or equal to 50 x 10^9/L for greater than or equal to 67% of bimonthly visits during weeks 14 to 24, were observed in 18% of those treated with fostamatinib versus 2% with placebo (P = .0003). An open-label extension of these 2 studies enrolled patients from FIT1 and FIT2 who either completed 24 weeks of therapy or did not respond to treatment after 12 weeks. Of 123 patients enrolled in the open-label extension, 27 (18%) achieved a stable response with a median duration over 28 months, 64 (44%) had an overall response, and 24 of 71 patients whose prior TPO-RA therapy failed achieved an overall response. The most common AEs occurring in more than 10% of patients included diarrhea, hypertension, nausea, epistaxis, and abnormal liver function tests. As fostamatinib is associated with hyperten-
sion, blood pressure should be monitored every 2 weeks until blood pressure is stable. Once controlled, monitoring can occur monthly, along with assessment of liver function tests and white blood cell count. Hypertension of any severity occurred in 28% of patients in clinical trials, with hypertensive crisis occurring in 1% of patients. Patients should be counseled on the potential for diarrhea, neutropenia, and concerns for fetal toxicity. Addi-

Role of the Pharmacist in Managing Patients With ITP
The management of ITP is highly individualized, and pharmacists in several practice settings have the opportunity to impact patient care along the spectrum of treatment. Armed with knowledge of available clinical practice guidelines and a firm understanding of available therapies, pharmacists in both the inpatient and outpatient settings can assist in therapy selection, confirm appropriate dosing, and ensure appropriate supportive care measures are taken. Addition-

### TABLE 2. PATIENT COUNSELING PEARLS FOR SELECT ITP THERAPIES

<table>
<thead>
<tr>
<th>Medication(s)</th>
<th>Medication class</th>
<th>Place in therapy</th>
<th>Lab monitoring</th>
<th>Counseling pearls and/or practical considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone, prednisone, prednisolone</td>
<td>Corticosteroid</td>
<td>Newly diagnosed ITP; may be used in acute episodes of persistent/chronic ITP</td>
<td>Platelet count, absolute lymphocyte count, glucose</td>
<td>• Use for the shortest period of time to limit AEs • Take with food in the morning • Consider gastric prophylaxis with acid suppressants for prolonged courses • Consider <em>Pneumocystis jirovecii</em> pneumonia prophylaxis for prolonged courses</td>
</tr>
<tr>
<td>Anti-D immune globulin</td>
<td>Immune globulin</td>
<td>Newly diagnosed ITP; may be used in acute episodes of persistent/chronic ITP</td>
<td>Platelet count, hemoglobin</td>
<td>• Patients must be Rh+, non-splenectomized, DAT-negative, and have adequate hemoglobin (&gt;9-10 grams/dL) • Premedicate with high-dose corticosteroid</td>
</tr>
<tr>
<td>IVIG</td>
<td></td>
<td>Newly diagnosed ITP; may be used in acute episodes of persistent/chronic ITP</td>
<td>Platelet count, absolute neutrophil count</td>
<td>• Consider scheduling acetaminophen x 24 hours after dose • Transient and self-limiting neutropenia may occur in the first week post-dose</td>
</tr>
<tr>
<td>Avatrombopag</td>
<td>Thrombopoietin receptor agonist</td>
<td>Chronic ITP(^a)</td>
<td>Platelet count</td>
<td>Take with food</td>
</tr>
<tr>
<td>Eltrombopag</td>
<td></td>
<td>Persistent and chronic ITP</td>
<td>Platelet count, liver function tests</td>
<td>Food and/or medications/supplements containing calcium, iron, or magnesium should be separated by at least 2 hours before or 4 hours after eltrombopag dose</td>
</tr>
<tr>
<td>Romiplostim</td>
<td></td>
<td>Persistent and chronic ITP</td>
<td>Platelet count</td>
<td>• Available as single-dose vials that require reconstitution • Do not shake the vials</td>
</tr>
<tr>
<td>Fostamatinib</td>
<td>Spleen tyrosine kinase inhibitor</td>
<td>Chronic ITP</td>
<td>Platelet count, liver function tests, blood pressure, absolute neutrophil count</td>
<td>• Can be taken with or without food • Initiate early supportive measures for diarrhea; report severe diarrhea</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Anti-CD20 monoclonal antibody</td>
<td>Persistent and chronic ITP; has been studied in newly diagnosed ITP(^b)</td>
<td>Platelet count, hepatitis B serologies, immunoglobulin levels</td>
<td>Generally administered weekly x 4 doses</td>
</tr>
</tbody>
</table>

AE, adverse effect; DAT, direct antiglobulin test; ITP, immune thrombocytopenia; IVIG, intravenous immunoglobulin.

\(^a\)Not FDA approved for persistent ITP.

\(^b\)Several studies have evaluated use of rituximab in upfront therapy in adult patients with favorable response rates, but its use in this setting is not currently recommended in either American Society of Hematology or international consensus report 2019 guidelines.
ally, pharmacists can assess lab values to titrate doses of agents appropriately. Health-system pharmacists are ideally positioned to provide education to the health care team and patients to ensure therapy selection aligns with patient preference. Additionally, pharmacists can assist in medication adherence strategies.39-41

Regardless of therapy, dispensing pharmacists in specialty and community pharmacies are ideally positioned to provide patients and caregivers with invaluable counseling and follow-up to ensure that the therapy is deployed in a safe and effective manner, and also assist with medication adherence strategies. Pharmacists are able to conduct medication reviews to ensure there are no drug–drug interactions or medications that may compromise platelet count. Similarly, for those patients established on therapy, ambulatory pharmacists are ideally positioned to oversee dose adjustments based on platelet responses and/or AE monitoring. A summary of the therapies likely to be encountered in patients with ITP, along with counseling points and practical considerations for use, are provided in Table 2.1,7,8,20,25-27,38

**Conclusion**

ITP can affect both adult and pediatric patients, and acute and long-term treatments may be needed. Although low platelet counts and corresponding hemostatic sequelae are a major focus of treatment, nonhemostatic symptoms can also have a significant negative impact on patient quality of life and may drive treatment decisions. Treatment of ITP is considered in phases (ie, newly diagnosed, persistent, and chronic), and multiple comprehensive clinical practice guidelines exist to guide therapy decisions. Treatment of newly diagnosed ITP consists of therapies aimed at halting autoimmune platelet destruction, while treatment of persistent/chronic ITP focuses on immunosuppression and/or therapies enhancing platelet production (eg, TPO-RAs). Most available therapies have significant monitoring and patient counseling ramifications, and pharmacists in many practice settings can play an impactful role in the care of patients with ITP.

**ADDITONAL RESOURCES**

| Platelet Disorder Support Association | www.pdsa.org/ |
| Foundation for Women & Girls with Blood Disorders | www.fwgbd.org/resources/ | itpresources |
| American Society of Hematology | www.hematology.org/ |

**REFERENCES**

10.1007/s10555-017-9677-x


INSTRUCTIONS FOR EARNING CREDIT

Begin the activity by reading the content in its entirety.

Go to www.pharmacytimes.org/go/ITP to access the online version of this activity.

Click “Proceed,” then complete the online pretest.

Once completed, click “Next” until reaching the activity posttest.

Complete the online posttest and activity evaluation form.

After successfully completing the posttest and evaluation form, this information will be uploaded to CPE Monitor.

You must complete these steps before the activity expires in order to receive your credit.

You may view your credit within 48 hours at www.mycpemonitor.net.

NOTE: Your CE credit will be automatically uploaded to CPE Monitor. Please ensure that your Pharmacy Times® account is updated with your NABP e-profile ID number and your date of birth. Participation data will not be uploaded into CPE Monitor if you do not have your NABP e-profile ID number and date of birth entered into your profile on www.pharmacytimes.org.

SYSTEM REQUIREMENTS FOR COMPLETION:
Computer or smartphone with internet-access web browser (IE7.0+ or Webkit-/Mozilla-compatible) with JavaScript enabled.

FOR QUESTIONS ABOUT THIS INTERNET CPE ACTIVITY, PLEASE CONTACT: ceinfo@pharmacytimes.com.

PRIVACY POLICY AND TERMS OF USE INFORMATION: www.pharmacytimes.org/terms.

EDUCATIONAL DISCLAIMER: Continuing professional education (CPE) activities sponsored by Pharmacy Times Continuing Education™ are offered solely for educational purposes and do not constitute any form of professional advice or referral. Discussions concerning drugs, dosages, and procedures may reflect the clinical experience of the author(s) or they may be derived from the professional literature or other sources and may suggest uses that are investigational in nature and not approved labeling or indications. Participants are encouraged to refer to primary references or full prescribing information resources.
POSTTEST QUESTIONS

1. Two months ago, a 37-year-old patient presented to clinic with an incidental finding of platelet count of 47 x 10^9/L and was asymptomatic. Other reasons for thrombocytopenia were ruled out, and a diagnosis of primary immune thrombocytopenia (ITP) was made. On evaluation today, the platelet count is 42 x 10^9/L. Using the international working group (IWG) definition, which of the following characterizes the patient’s diagnosis?  
   A. Acute ITP  
   B. Newly diagnosed ITP  
   C. Persistent ITP  
   D. Chronic ITP  

2. TJ is a 22-year-old man initiating fostamatinib for chronic ITP. Which counseling point should be shared with him?  
   A. Take with food  
   B. Diarrhea may occur  
   C. Avoid calcium-containing products  
   D. Monitoring of blood glucose required  

3. KR is a 64-year-old man with primary ITP diagnosed 9 months ago who continues to have a platelet count of 30 x 10^9/L. Which term most accurately describes the current status of his ITP?  
   A. Newly diagnosed ITP  
   B. Refractory ITP  
   C. Chronic ITP  
   D. Persistent ITP  

4. OM is a 55-year-old woman presenting with significant epistaxis, a hemoglobin of 7.5 grams/dL, and a platelet count of 9 x 10^9/L. A diagnosis of ITP is made and the medical team and patient would like to initiate treatment. Which of the following is the most appropriate initial treatment?  
   A. Anti-D immune globulin 75 mcg/kg IV x 1 dose  
   B. Avatrombopag 20 mg by mouth daily  
   C. Dexamethasone 40 mg by mouth daily x 4 days  
   D. Romiplostim 1 mcg/kg subcutaneous x 1, repeat weekly  

5. JK is a 32-year-old man with chronic ITP treated with avatrombopag 20 mg by mouth daily. Most recent platelet counts have been 298 x 10^9/L and 312 x 10^9/L, with no bleeding symptoms. What dose of avatrombopag would be most appropriate?  
   A. 20 mg by mouth 3 times weekly  
   B. 20 mg by mouth daily  
   C. 40 mg by mouth daily  
   D. 10 mg by mouth daily  

6. Per the IWG, what defines severe ITP?  
   A. Platelets <20 x 10^9/L  
   B. Platelets <30 x 10^9/L  
   C. Bleeding not requiring treatment, platelets <30 x 10^9/L  
   D. Bleeding requiring treatment regardless of platelet count  

7. Which of the following is an oral thrombopoietin receptor agonist that should be taken with food?  
   A. Avatrombopag  
   B. Eltrombopag  
   C. Fostamatinib  
   D. Romiplostim  

8. CC is a 3-year-old girl with chronic ITP unresponsive to romiplostim 10 mcg/kg. Her hematologist would like to switch her thrombopoietin receptor agonist and start eltrombopag. Which of the following is the most appropriate starting dose?  
   A. 12.5 mg by mouth daily  
   B. 25 mg by mouth daily  
   C. 50 mg by mouth daily  
   D. 75 mg by mouth daily  

9. JL is a 68-year-old woman who presents to clinic for follow up for primary ITP and osteoporosis, for which she takes calcium, vitamin D, and alendronate. She did not respond to steroid therapy, and wants to avoid injections as much as possible. Which of the following would be most appropriate to consider?  
   A. Avatrombopag  
   B. Eltrombopag  
   C. Romiplostim  
   D. Vincristine  

10. Which of the following supplements should be separated by at least 2 hours before or 4 hours after administration of eltrombopag?  
    A. Potassium  
    B. Iron  
    C. Zinc  
    D. Folate
Risks of Respiratory Syncytial Virus in Older Adults: Emerging Prophylactic Vaccines and Intervention Opportunities for Pharmacists

Overview of Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) has been shown to affect older adults at a high rate with a significant risk of mortality. In addition, RSV is one of the most common viruses to infect children worldwide. RSV commonly presents as an upper respiratory tract infection that usually results in mild, cold-like symptoms that resolve in 1 to 2 weeks. Symptoms include nasal congestion, rhinorrhea, cough that can progress to wheezing, sneezing, and fever. RSV can be serious. A significant but minority number of patients subsequently develop lower respiratory tract infections.

In infants and children younger than 1 year, RSV is the most common viral cause of lower respiratory tract infections including bronchiolitis and pneumonia. In the United States, it is estimated that 170,000 to 177,000 older adults are hospitalized, with 14,000 to 17,000 deaths each year related to RSV infection. Of the deaths, a United Kingdom modeling study found that 93% are in individuals 65 years and older. In addition, it is estimated that RSV causes 12% of acute respiratory illnesses in individuals older than 50 years, and approximately 2% to 10% of community-dwelling adults can be infected with RSV at any one time.

Although RSV is typically thought of as a pediatric infection, older adults experience significant morbidity and mortality. In the United States, it is estimated that 170,000 to 177,000 older adults are hospitalized, with 14,000 to 17,000 deaths each year related to RSV infection. Of the deaths, a United Kingdom modeling study found that 93% are in individuals 65 years and older. In addition, it is estimated that RSV causes 12% of acute respiratory illnesses in individuals older than 50 years, and approximately 2% to 10% of community-dwelling adults can be infected with RSV at any one time.

EDUCATIONAL OBJECTIVES

At the completion of this activity, the participant will be able to:
- Determine the pathology, symptomatology, and diagnosis of respiratory syncytial virus (RSV)
- Explore the latest information on the safety, efficacy, administration, and dosing of the emerging vaccines for RSV
- Examine the role of the pharmacist in the management of RSV, including adult patient education on current preventive methods and emerging vaccines

TARGET AUDIENCE: Community pharmacists

ACTIVITY TYPE: Application

RELEASE DATE: August 16, 2021

EXPIRATION DATE: August 16, 2022

ESTIMATED TIME TO COMPLETE ACTIVITY: 2.0 hours

FEE: This lesson is offered for free at www.pharmacytimes.org.

The animation provides a visual overview of RSV and its burden, while highlighting key points. Accompanying this activity are video vignettes that feature a pharmacist providing education and recommendations to patients about the prevention of RSV. Both components can be accessed at pharmacytimes.org/go/RSV.

The tear out provides a quick reference on RSV to equip pharmacists with a useful tool to help counsel their patients.

Pharmacy Times Continuing Education™ is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education. This activity is approved for 2.0 contact hours (0.20 CEUs) under the ACPE universal activity number 0290-0000-21-288-H01-P. The activity is available for CE credit through August 16, 2022.

The following contributors have no financial relationships with commercial interests to disclose:

FACULTY
Miranda Wilhelm, PharmD
Clinical Professor
Southern Illinois University Edwardsville (SIUE) School of Pharmacy
Department of Pharmacy Practice
Edwardsville, Illinois

DISCLOSURES
The following contributors have no financial relationships with commercial interests to disclose:

FACULTY
Miranda Wilhelm, PharmD

PHARMACY TIMES CONTINUING EDUCATION™

PLANNING STAFF
Jim Palatine, RPh, MBA; Maryjo Dixon, RPh; Dipi Desai, PharmD, CHCP; Liza Patel, PharmD, RPh; Crissy Wilson; Liz Rauh; Susan Pordon; Brianna Winters; and Chloe Taccetta

PHARMACY TIMES® EDITORIAL STAFF
Davy James

An anonymous peer reviewer was part of the content validation and conflict resolution and has no financial relationships with commercial interests to disclose.
Comorbidities also contribute to the morbidity and mortality related to RSV infections for older adults. RSV has been identified as a growing cause of respiratory disease in older adults, particularly among those who are immunocompromised, have underlying chronic cardiopulmonary conditions, and are considered frail, elderly patients. In those who are immunocompromised, RSV pneumonia rates could be as high as 80%, with approximately 70% to 80% of those cases being fatal.\(^8\) RSV infection is a common cause of exacerbation of chronic obstructive pulmonary disease (COPD) and heart failure.

In hospitalized patients, RSV is detected in approximately 10% of respiratory illnesses and is associated with a 10% case fatality rate.\(^9\) A study using laboratory surveillance data from Arizona found the percentage of RSV cases among adults 65 years or older statistically increased from 4% in 2013 to 11% in 2017 (\(P < .001\)).\(^7\) Older adults had more than 8 times the odds of a positive RSV test result than children younger than 5 years.\(^7\) Although this increase in incidence is probably the result of changes in testing practices and sensitivities of viral diagnostic tests, it highlights that older adults are at risk for RSV infection.

As of 2019, there was a global estimate of 703 million individuals older than 65 years, with numbers expected to increase in the coming decades.\(^10\) The aging of the global population illustrates the need for effective RSV treatments and prophylactic vaccines, especially for older adults.

On June 10, 2021, the CDC issued an official health advisory alerting providers and caregivers about increased interseasonal RSV activity across the southern United States.\(^11\) RSV activity in 2020 decreased rapidly, likely due to the public health measures implemented to reduce the spread of SARS-CoV-2.\(^11\) However, in late March 2021, RSV activity began to increase. The percentage of positive RSV tests went from less than 5% at the end of February 2021 to more than 25% at the start of June 2021.\(^12\) This coincides with the lifting of public health measures due to reduced RSV circulation during the winter months, infants and children who had previously not been exposed to RSV might now be at increased risk for infection. The CDC was advising providers to consider RSV infection in patients testing negative for SARS-CoV-2 with acute respiratory symptoms and encouraged laboratory testing.\(^11\)

Accompanying the morbidity and mortality of clinical disease is the significant economic burden. In the United States, costs for RSV are estimated at $342 million annually, with $150 million to $160 million related to pneumonia in older adults alone.\(^8,13\) If costs associated with exacerbations of chronic medical conditions were included, the numbers would be higher.

### Treatment approach

Currently, there are limited effective pharmacologic treatment options for RSV infection. Symptom management using nasal suction and lubrication for congestion, antipyretics for fever reduction, hydration (oral or intravenous), nonprescription cough/cold products for nasal congestion and rhinorrhea, bronchodilators for wheezing, and oxygen therapy for patients experiencing hypoxia provide supportive care.\(^14\) Patients presenting with severe disease including respiratory failure may require high-flow nasal cannula, continuous positive airway pressure, intubation, and mechanical ventilation.\(^14\) Passive immune prevention is available as a monoclonal antibody, palivizumab, that has activity against the RSV membrane fusion protein.\(^14\) Palivizumab must be administered monthly throughout the RSV season. Aerosolized ribavirin is the only antiviral medication approved for use against RSV; however, there is controversy around its use due to the cost versus benefit, danger to exposed health care providers, and questions of efficacy, specifically regarding mortality, length of mechanical ventilation, and length of hospital stay.\(^14\)

In addition, transmission prevention strategies (eg, washing hands, covering coughs/sneezes, avoiding close contact with infected individuals, and cleaning frequently touched surfaces) are the mainstay. There is an urgent need for RSV prevention strategies to reduce morbidity and mortality, especially in older adults. While no RSV vaccine is currently available, several candidates have been developed and are in various stages of clinical trials. The purpose of this article is to educate pharmacists on commonalities and risk factors about RSV in older adults.
adults while understanding the profile and future benefit of RSV vaccine candidates.

Pathology, Symptomatology, and Diagnosis of Respiratory Syncytial Virus

RSV is an enveloped, negative-sense, single-stranded, RNA virus that belongs to the Pneumoviridae family, genus Ortho-pneumoviridae. See FIGURE 1. The virus has 3 surface proteins that are important for viral infectivity of the host cell, natural immunity, and potential therapeutic targets for vaccine development. The 3 surface proteins are G (attachment), F (fusion), and SH (small hydrophobic-proposed viroporin). Attachment triggers the F-surface protein to change conformations folding from a prefusion (preF) to a postfusion (postF) configuration. The F-surface protein postfusion configuration initiates viral penetration into the host cell by fusing the viral and host cell membranes. Understanding the 2 F-protein conformations has been imperative in therapeutic intervention development.

The preF is the active form of the surface protein but is easily triggered to fold into the postF configuration. The postF conformation is very stable and cannot return to the preF form. The folding rearrangement changes the availability of antigenic sites, as targets on the preF conformation are not the same as those on the postF conformation. Results of studies have found antibodies that bind to preF are more efficient at neutralizing RSV than those shared by both preF and postF conformations. This helps direct opportunities for vaccine targets as well as neutralizing monoclonal antibody development. In addition, the preF site is the preferred target for therapeutic intervention due to its essential role in viral entry into the host cell, similar structure between RSV A and B groups, and that it carries several antigenic sites that elicit high potency neutralizing antibodies.

RSV is divided into 2 major antigenic groups, A and B, due to variability on the G-surface protein. The A and B groups can be further subdivided into 13 RSV A genotypes and 20 RSV B genotypes. Strains of both groups generally circulate simultaneously during the same season, but the proportions of A and B vary on a yearly basis.

Similarly to influenza, RSV typically circulates following a seasonal pattern, with peaks in fall to winter each year, but this can vary depending on geographic location. Transmission occurs via viral shedding of nasopharyngeal secretion droplets that enter the mouth, nose, and eyes or via autoinoculation from contaminated surfaces. RSV can remain stable on nonporous environmental surfaces for up to 6 hours, gloves for 90 minutes, paper for 30 to 45 minutes, and skin for 20 minutes. Direct person-to-person contact or contact with contaminated environmental surfaces are the most common routes of transmission. For adults, after inoculation, symptoms develop in 3 to 5 days. Viral shedding, where patients are infectious to others, occurs on average of 3 to 6 days with a range of 1 to 12 days.

Clinically, RSV may be difficult to distinguish from influenza and other respiratory viruses, such as common cold rhinoviruses and SARS-CoV-2. Presentation of RSV can vary with the patient’s age, health status, and whether the infection is primary or secondary. A typical timeline of signs and symptoms in adult patients with RSV is reviewed in FIGURE 2. In adults, RSV typically begins with nasal congestion and rhinorrhea or pharyngitis, which help to distinguish it from influenza. If the virus progresses into the lower respiratory tract, symptoms such as cough, wheezing, and dyspnea are common. Other
nonspecific symptoms such as anorexia and fever occur with varying severity.8,15 Symptoms of myalgias and malaise are more common with influenza than RSV infections.8

In contrast, infants and young children with RSV infection often initially present with rhinorrhea and a decrease in appetite before other symptoms appear.3 Onset of cough is usually 1 to 3 days later and soon after, sneezing, fever, and wheezing may occur.3 Irritability, decreased activity, and/or apnea may be the only signs of infection in very young infants.3

The diagnosis of RSV is typically done by physical examination and clinical expertise of the health care provider and does not require confirmatory laboratory testing or imaging. RSV bronchiolitis should be suspected in infants with lower respiratory tract disease, the winter season, and a known circulation of RSV in the community.19 RSV should also be suspected in patients hospitalized with an acute lower respiratory disease if they are immunocompromised or 65 years or older.15 However, other respiratory pathogens share the clinical pattern of RSV, and clinical features alone are insufficient to distinguish RSV from other infections.

Laboratory diagnosis of RSV should be pursued if the identification of RSV will affect the patient’s clinical management. When confirmation of RSV infection is necessary, testing is done by cell culture, serology, antigen detection tests, and real-time polymerase chain reaction (PCR).15 Cell culture is no longer recommended for primary diagnosis due to the length of time to receive results (3-5 days) and low sensitivity (17%-39%).15 Serology, the presence of IgM or IgG, is not clinically useful in adults.15 Rapid antigen detection and direct fluorescent antibody tests were designed as point-of-care tests with results in 15 to 30 minutes or 30 to 60 minutes, respectively.15 The sensitivities are low in adults (20%-70%), as these tests are intended for younger patients who would have higher viral loads for detection.15 This can result in false-negative results. PCR is the gold standard and favored over the other methods because of superior sensitivity (90.6%-97.9%), specificity (99.4%-100%), and length of time (1-2 hours) to results.15 A multiplex PCR, which tests for RSV and other pathogens with one panel, has become increasingly common for use in detection despite rapid antigen tests being less costly.17 Multiplex PCR may also distinguish RSV A and B serotypes.15 Both antigen and PCR testing are readily available.

A differential diagnosis may be made to identify pathogens that cause similar syndromes including bronchiolitis, pneumonia, bronchial reactivity, and lower respiratory tract disease in older adults and immunocompromised patients. The differential diagnosis will determine RSV from asthma, bronchiolitis, influenza, croup, bronchitis, and pneumonia.

### Emerging Vaccines for Respiratory Syncytial Virus

The goal of an RSV vaccine is to prevent severe disease and subsequent complications in those at high risk for infection.15 Target groups for vaccination include infants, young children, and older adults.15 In addition, to protect infants in the first few months of life prior to vaccination, new research has been directed at vaccination of pregnant women.15 Maternal vaccination would provide antibody transfer to the infant, conferring protection during the first months of life. Efforts to develop an RSV vaccine have been ongoing for decades, but with unsuccessful results. Reinfections throughout life are common, which demonstrates that immunity after natural infection is neither complete nor long lasting.4

It is important to note the initial attempts to develop an RSV vaccine candidate in the 1960s. The whole cell vaccine virus was produced in cell culture, inactivated by heat and formalin, and mixed with an adjuvant.4,15 While the vaccine was well tolerated, when RSV-naïve but vaccinated infants were exposed to natural RSV infection, they experienced enhanced RSV disease (ERD).15 Of those vaccinated who developed ERD, 80% required hospitalization and 2 died.3 Older children who had likely been exposed to a previous RSV infection, priming their immune system, did not experience ERD.4 Recent efforts have generated multiple vaccine candidates that show promise.

The World Health Organization (WHO) has identified 19 unique vaccine candidates that are currently active in evaluation consisting of phase 1 through 3 clinical trials.20 Several different approaches are being tried, including the use of live attenuated virus vaccines, subunit vaccines, vector-based vaccines, and nanoparticle vaccine approaches, each with advantages and disadvantages.20 Due to the large number of vaccine candidates in clinical trials, a representative sample of promising vaccines will be discussed. Many of the vaccines are still in earlier phases of clinical trials, and anticipated availability dates of the vaccines are not readily available at this time, but it is helpful for pharmacists to be aware of what may be on the horizon. A number of these investigational vaccine names are similar in nature and may be difficult to distinguish; to avoid any potential confusion among those listed, as is seen commonly with discussion of COVID-19 vaccines, manufacturer names have been included to help identify the different vaccines.
Live attenuated vaccines

Live attenuated vaccines use temperature, chemicals, or different types of gene alteration to modify the RSV, which discourages severe disease but still allows the virus to replicate, inducing an immune response. Most of the vaccine candidates are in phase 1 clinical trials. Advantages of live attenuated vaccines include promotion of both humoral and cellular immune responses and, for RSV, the possibility of administration via intranasal drops, which are less invasive and potentially better tolerated than an intramuscular injection for infants and children. Most of the research to date has been done in children aged 6 to 24 months with varying results as researchers try to determine which attenuation(s) provide the best immune response while minimizing the adverse effect profile. A disadvantage of live attenuated vaccines is the contraindication and precaution for use in patients who are immunocompromised or have chronic medical conditions. In addition, live attenuated vaccines will likely not be effective in older adults due to previous exposure to RSV and therefore preexisting immunity that will reduce viral replication, limiting the ability to generate adequate immunogenicity.

Subunit vaccines

Subunit vaccines are a type of inactivated vaccine that use a specific fragment of the virus, such as a protein, sugar, or capsid, to induce an immune response. Most of the vaccine candidates are in phase 1/2 clinical trials. Advantages of subunit vaccines include safety in pregnant women and older adults. Most of the research to date has been done in adults (18-64 years), specifically pregnant women, women of childbearing potential, and older adults. Vaccine candidates have used various antigenic sites of the preF protein conformation as researchers try to find the site that provides the best immune response while minimizing adverse effects. Disadvantages include induction of a primarily CD4 T cell-mediated cellular immunity, which places RSV seronegative infants at higher risk for vaccine-related ERD. In addition, the requirement of adjuvants and booster doses due to the nonreplicating nature and highly specific but limited vaccine components elicit an immune response.

RSVpreF (Pfizer)

Two randomized, placebo-controlled, phase 1/2, first-in-human trials in adults aged 18 to 85 and 50 to 85 years have been completed and terminated, respectively. The objective of the studies was to evaluate the safety, tolerability, and immunogenicity of up to 6 or 7 RSV vaccine formulations (low, medium, and high dose with and without an adjuvant) when administered alone or in combination with seasonal inactivated influenza vaccine. Inclusion criteria were healthy men and women aged 18 to 85 years. Exclusion criteria generally included chronic medical conditions (HIV, hepatitis B, hepatitis C), immunosuppression, hematologic abnormalities, history of severe adverse reaction to a vaccine, pregnancy or breastfeeding. Safety data reported most frequently were mild pain at injection site, which was seen more frequently in the 18- to 49-year age group compared with the 50- to 85-year age group. Most commonly reported systemic adverse reactions were mild to moderate fatigue and mild to moderate headache. Geometric mean titers for RSV A and B generally increased for all groups 2 weeks after vaccination and then slowly declined over the next 12 months. No results data were available on the terminated study in 50- to 85-year-old participants.

A phase 2b, multicenter, randomized, placebo-controlled trial evaluated the safety, tolerability, and immunogenicity of the RSVpreF vaccine (low dose or high dose with or without an adjuvant) in 650 pregnant participants. In addition, safety and characteristics of transferred antibodies to the infants will be measured. Inclusion criteria included healthy women aged 18 to 49 years who are 24 to 36 weeks gestation with an uncomplicated pregnancy. Exclusion criteria were extensive but generally included conditions associated with prolonged bleeding, history of a severe reaction to a vaccine, pregnancy as a result of in vitro fertilization, infection (HIV, hepatitis B, hepatitis C, syphilis), history of an autoimmune disease, treatment with immunosuppressive therapy, and breastfeeding. Although data from this study have not been published, Pfizer issued a press release in June 2020 stating that results of a phase 2b proof-of-concept study of RSVpreF in pregnant women were positive. The positive results support use of the vaccine in a phase 3 clinical trial.

The phase 3, multicenter, randomized, double-blind, placebo-controlled study is targeting enrollment of 10,000 participants. The objective of the study is to evaluate the efficacy, safety, and immunogenicity of RSVpreF versus placebo (1:1 ratio) in infants born to women vaccinated during pregnancy. In addition, the safety and immunogenicity in pregnant women will be studied. Primary study outcomes will be measured by relative risk reduction in the incidence of lower respiratory tract infection due to RSV in infants through 180 days of life whose mothers were vaccinated compared with the placebo group. Inclusion criteria include pregnant women 49 years or younger who are 24 to 36 weeks gestation with a singleton, uncomplicated preg-
nancy. Select exclusion criteria include prepregnancy BMI greater than 40 kg/m², any condition associated with prolonged bleeding, history of severe adverse reaction to a vaccine, pregnancy as a result of in vitro fertilization, and previous or current pregnancy complications (e.g., preeclampsia, thyroid disorders, diabetes). No details about the dose of RSVpreF were included with the ClinicalTrials.gov protocol. The study is currently recruiting with an estimated completion date of November 2023.

**GSK3888550A (GlaxoSmithKline)**

GlaxoSmithKline has 2 subunit vaccine candidates: one that is being studied for maternal immunization and one that is being studied in adults aged 60 to 80 years.

The goal of GSK3888550A is to prevent RSV-associated lower respiratory tract infections in infants during the first months of life via maternal antibody transfer. A phase 1, multicenter, randomized, placebo-controlled, observer-blind study enrolled 502 healthy, nonpregnant women aged 18 to 45 years to evaluate various doses (30 mcg, 60 mcg, 120 mcg) of the vaccine. The objective of the study was to evaluate the safety, reactogenicity, and immunogenicity of the RSVpreF3 vaccine in nonpregnant women as preparation for a study use in pregnant women.

Inclusion criteria included healthy women of childbearing potential, aged 18 to 45 years. Exclusion criteria included immunosuppressant condition or therapy, chronic medical conditions (e.g., diabetes, COPD, uncontrolled asthma, psychiatric illness, neurologic disease, cardiovascular disease, hepatitis B, hepatitis C), BMI greater than 40 kg/m², pregnancy or breastfeeding, and acute infection. The vaccine demonstrated a rapid boost in preexisting immunity at all doses. High levels of protective neutralizing antibodies were produced, and by day 8 there was a 14-fold increase in RSV A and B neutralizing antibody titers observed. While titers declined over time, a greater than 6-fold increase was still maintained at day 91. Overall, the vaccine was well tolerated with no safety concerns identified. The most common adverse effects reported were minor pain at the injection site and headache. The positive results of this study support use of the vaccine in phase 2 and clinical trials.

The GRACE study, a phase 3, randomized, double-blind, placebo-controlled, multicenter clinical trial targeting enrollment of 20,000 pregnant women aged 18 to 49 years, was initiated on November 20, 2020. This is the phase 3 trial that resulted from the positive results of GSK3888550A discussed above. The objective of the study is to evaluate the ability of GSK3888550A RSV single-dose vaccine to prevent lower respiratory tract infections in infants born to vaccinated mothers.

The study will also evaluate the safety of the vaccine in the vaccinated mothers and infants. The unadjuvanted vaccine will be administered intramuscularly. The study is currently recruiting and is estimated to end in February 2024 with interim results anticipated in the second half of 2022.

**GSK3844766A (GlaxoSmithKline)**

A phase 1/2, randomized, observer-blind study assessed the safety, reactogenicity, and immunogenicity of the RSV candidate vaccine, GSK3844766A, in older adults. The study is being conducted in 2 parts: part 1 is young adults aged 18 to 40 years and part 2 is older adults aged 60 to 80 years. The vaccine was a 2-dose series with various antigen doses (low, medium, and high dose with and without an adjuvant) administered intramuscularly according to a 0, 2-month schedule compared with placebo. The adjuvant is AS01, which is also used in the recombinant zoster vaccine. The inclusion criteria were fairly open as long as participants met the age requirements. Exclusion criteria were extensive and included use of any investigational product, immunosuppressant status via drugs or medical condition, history of allergic reaction to a vaccine, unstable chronic medical conditions (diabetes, hypertension, COPD), history of neurologic disorder, BMI greater than 40 kg/m², laboratory result abnormalities, and pregnancy or breastfeeding. One month post immunization, the vaccine produced a robust humoral and cellular immune response compared with baseline. The vaccine elicited a near 10 times increase of RSV A protective antibodies and more than 12 times increase in RSVpreF3 IgG antibodies. Additionally, cellular response and immunity in older adults reached similar ranges observed in young adults, demonstrating the vaccine can stimulate the immune system in older adults. An extension of this study is currently recruiting participants to receive the RSV vaccine approximately 18 months after they received their respective second dose in the parent study.

A randomized, open-label, phase 3 trial, AReSVi 004, assesses the safety, reactogenicity, and long-term persistence of immune responses up to 3 years following vaccination with a single dose of GSK3844766A in adults 60 years and older. The study will also evaluate immune responses of additional vaccine doses given according to different revaccination schedules. The study is estimated to be completed in June 2024 with interim results anticipated in the second half of 2022.

A second study, AReSVi 006, is expected to begin enrolling patients to investigate the efficacy of the GSK3844766A vaccine to help protect older adults against lower respiratory tract infections.
Vector-based vaccines

Vector vaccines use a nonreplicating modified version of a different virus as a carrier to deliver RSV proteins as an antigen to elicit an immune response, capitalizing on the adjuvant effect of the vector. Most of the vaccine candidates are in phase 1 or 2 clinical trials. Advantages of vector-based vaccines include a well-established vaccine platform that elicits a strong humoral and cell-mediated immune response. In addition, there is no risk of ERD in pediatric patients. Disadvantages include previous exposure to the vector could result in reduced effectiveness. In this case, the immune system recognizes the vector and destroys it before the vector has a chance to deliver the vaccine antigen.

MVA-BN RSV (Bavarian Nordic)

MVA-BN RSV is a nonreplicating modified vaccinia Ankara virus previously used as a vaccine against smallpox. The vaccine displays the RSV surface proteins F and G (for both A and B serotypes) and 2 internal RSV proteins, N and M2. A phase 1 study demonstrated that the vaccine was well tolerated and induced both humoral and cellular immunity. This led to a randomized, single-blind, placebo-controlled, phase 2 trial to evaluate the vaccine’s safety and immunogenicity in adults 55 years and older. The trial enrolled 420 participants divided into multiple groups to identify the optimal dose (single low dose, 2 low doses, single high dose, 2 high doses) and vaccination schedule. In addition, a subgroup will receive a booster dose 1 year after the first vaccination. Inclusion criteria included men and women 55 years and older, stable chronic medical conditions, BMI greater than or equal to 18.5 and less than or equal to 39.9 kg/m², and laboratory values within normal limits. Exclusion criteria included infection (acute, HIV, hepatitis B, hepatitis C), pregnancy or breastfeeding, autoimmune disease, allergic reaction to a vaccine, and use of immune-modifying drugs. The safety results show the vaccine was well tolerated with no vaccine-related serious adverse effects being reported.

A single dose increased neutralizing (RSV A and B) and total (IgG and IgA) antibodies 1.6 to 2.4-fold from baseline. The vaccine elicited a persistent immune response for at least 6 months and revaccination at 12 months showed a booster response. A phase 3 trial in older adults is planned for initiation in 2021.

Ad26.RSV.preF (Janssen)

Ad26.RSV.preF is a nonreplicating adenovirus vector vaccine that delivers the RSV fusion protein as the antigen. This uses the same adenovirus vector technology platform as the Janssen/Johnson & Johnson COVID-19 vaccine. A phase 1 study demonstrated that the vaccine was well tolerated and induced both humoral and cellular immunity in adults 60 years and older. The geometric mean titers were maintained above baseline levels 2 years after immunization and displayed a booster effect with a second immunization at 1 year.

A phase 2a, double-blind, placebo-controlled study assessed the safety and efficacy of Ad26.RSV.preF administered in combination with influenza vaccine in 180 participants 60 years and older. Overlapping RSV and influenza seasons presents an opportunity for coadministration of vaccines for both infections. Participants received both vaccines on day 1 followed by placebo on day 29 or placebo plus influenza day 1 followed by Ad26.RSV.preF on day 29. The immune response to the influenza vaccine met criteria for noninferiorty. Both groups had robust neutralizing antibody response to the RSV vaccine. The authors concluded that simultaneous administration of influenza and Ad26.RSV.preF RSV vaccines is compatible.

A phase 2, randomized (1:1 ratio), double-blind, placebo-controlled study in 53 healthy adults aged 18 to 50 years evaluated if a single dose of Ad26.RSV.preF could protect participants from RSV infection and disease via a human challenge model. Twenty-eight days after receipt of the vaccine, participants were challenged intranasally with RSV A. The primary end point was post-challenge RSV viral load measured by PCR. The results showed significantly lower viral loads in the vaccinated group versus the placebo group (P = .012). In addition, geometric mean antibody titers increased 5.8-fold (95% CI, 4.4–7.8) in the vaccinated group while remaining similar in the placebo group. No vaccine-related serious adverse effects were reported. The authors concluded that the study demonstrated protection from RSV infection through immunization and hypothesized that this could result in protection against natural RSV infection and disease. This is the first study to assess the proof of concept for vaccine-mediated protection against RSV infection.

ChAd155-RSV (GlaxoSmithKline)

ChAd155-RSV is a nonreplicating chimpanzee adenovirus vector vaccine that delivers the RSV F, N, and M2-1 proteins as the antigen to elicit an immune response. A first-in-human, phase 1, randomized, observer-blind, placebo- and active-control study evaluated the safety and immunogenicity of the ChAd155-RSV vaccine in healthy adults aged 18 to 45 years. Participants received 2 injections (low dose, high dose, active comparator [meningococcal group B vaccine], or placebo) administered intramuscularly at 0 and 1 month. The authors concluded that the vaccine was well tolerated.
tolerated and induced both humoral and cellular immunity with no safety concerns.\(^{41}\)

A phase 1/2, randomized study evaluated the safety, reactogenicity, and immunogenicity of ChAd155-RSV in RSV-seropositive infants aged 12 to 23 months.\(^{42}\) The study evaluated a 2-dose series with various antigen doses (low, medium, and high dose) administered intramuscularly with a 0, 1-month schedule. Inclusion criteria included boys or girls, seropositive status for RSV, and full-term birth.\(^{42}\) Exclusion criteria were extensive and included immunosuppressed status, receipt of blood products, acute or chronic medical conditions, congenital defects, neurologic disorders, HIV-positive mother, wheezing, cough, history of adverse reaction to a vaccine, and acute infection.\(^{42}\) The trial has been completed but results have not been published at this time.\(^{42}\)

### Nanoparticle vaccines

Nanoparticle vaccines are synthesized by using recombinant DNA technology to produce multiple copies of a modified RSV protein expressed on the surface of the particle, which induces an immune response.\(^{21}\) The antigens exposed on the surface of the particle mimic the native viral surface proteins. Most of the vaccine candidates are in phase 1 or 2 clinical trials. Advantages of nanoparticle vaccines include strong humoral and cellular immune response in addition to safety due to the lack of virus particles in the vaccine.\(^{21}\)

#### RSV F nanoparticle (Novavax)

RSV F is a nanoparticle matric composed of recombinant RSV postF configuration proteins as the antigen to elicit an immune response.\(^{21}\) The vaccine is being evaluated in pregnant women, children (2-6 years old), and older adults (≥60 years old).

Phase 1 and 2 clinical trials demonstrated that the vaccine was well tolerated and highly immunogenic in the older adult population studied.\(^{21}\) This prompted RESOLVE, a phase 3, randomized, observer-blinded, placebo-controlled trial to evaluate the efficacy of RSV F vaccine in adults 60 years and older.\(^{43}\) The primary objective was to demonstrate efficacy of a single dose of vaccine in prevention of moderate to severe RSV lower respiratory tract infections.\(^{44}\) The study enrolled 11,856 participants to receive 135 mcg of the vaccine via intramuscular injection or placebo.\(^{43,44}\) The results of the study failed to meet prespecified efficacy objectives. Vaccine efficacy was reported as −7.9% (95% CI, −84 to 37; \(P = .78\)).\(^{44}\) Similar numbers of participants in the vaccine (n = 28) and placebo (n = 26) groups developed moderate to severe RSV-associated lower respiratory tract infections.\(^{44}\) However, the vaccine did show a 61% reduction in hospitalizations due to COPD exacerbations.\(^{21}\)

The unsuccessful results of the RESOLVE trial prompted a second phase 2 clinical trial in older adults. The study evaluated the safety and immunogenicity of a single or 2-dose regimen of the RSV F vaccine with and without adjuvants (aluminum phosphate or Matrix-M) in 300 older adult participants.\(^{45}\) All vaccine doses were well tolerated.\(^{45}\) The inclusion of adjuvants increased the magnitude, duration, and quality of the immune response compared with the nonadjuvanted vaccine in both the single and 2-dose regimens.\(^{45}\) The data support continued research using adjuvanted vaccine formulations.

<table>
<thead>
<tr>
<th>Vaccine type</th>
<th>Vaccine name</th>
<th>Sponsor</th>
<th>Study population</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subunit</td>
<td>RSVpreF</td>
<td>Pfizer</td>
<td>Adults, Pregnant women, Older adults</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>GSK3888550A</td>
<td>GlaxoSmithKline</td>
<td>Pregnant women</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>GSK3844766A</td>
<td>GlaxoSmithKline</td>
<td>Older adults</td>
<td>IM</td>
</tr>
<tr>
<td>Vector-based</td>
<td>MVA-BN RSV</td>
<td>Bavarian Nordic</td>
<td>Older adults</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>Ad26.RSV.preF</td>
<td>Janssen</td>
<td>Older adults</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>ChAd155-RSV</td>
<td>GlaxoSmithKline</td>
<td>Children</td>
<td>IM</td>
</tr>
<tr>
<td>Nanoparticle</td>
<td>RSV F nanoparticle</td>
<td>Novavax</td>
<td>Children, Pregnant women, Older adults</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>ResVax</td>
<td>Novavax</td>
<td>Pregnant women</td>
<td>IM</td>
</tr>
</tbody>
</table>
ResVax (Novavax)

ResVax is an RSV F nanoparticle vaccine that contains an aluminum phosphate adjuvant being developed as a maternal immunization to protect infants from RSV. Phase 1 and 2 clinical trials demonstrated the vaccine effectively transfers RSV neutralizing antibodies to infants when pregnant women received the vaccine in the third trimester. The vaccine then moved into the phase 3 PREPARE trial; a randomized, placebo-controlled, observer-blind, multicountry study to evaluate the efficacy of maternal immunization with the vaccine in the prevention of RSV lower respiratory tract infection during the first 90 to 180 days of an infant’s life. The study enrolled 4363 pregnant women at 28 through 36 weeks gestation with an expected delivery date near the start of RSV season. Participants received a single dose of the RSV F nanoparticle vaccine or placebo. Criteria for success of the primary end point was prespecified at the lower bound 97.5% CI of greater than or equal to 30%. Results for vaccine efficacy for RSV-associated medically significant lower respiratory tract infection was 39.4% (vaccine: 97.5% CI, −1.0 to 63.7; placebo: 95% CI, 5.3-61.2). Vaccine efficacy for reducing RSV-related severe hypoxemia was 48.3% (5% CI, −8.2 to 75.3). Vaccine efficacy for RSV-associated lower respiratory tract infection hospitalizations was 44.4% (95% CI, 19.6-61.5). The study failed to meet the prespecified primary outcome of prevention of medically significant lower respiratory tract infection, although RSV-associated hypoxemia and hospitalizations were reduced. Of note, infants born to women who received the vaccine in the third trimester received the vaccine in the third trimester were approximately 50% less likely to have pneumonia reported compared with those in the placebo group. Because the vaccine failed to achieve the primary outcome, the Food and Drug Administration (FDA) and European Medicines Agency recommended the manufacturer conduct an additional phase 3 clinical trial to confirm efficacy of the vaccine.

**TABLE 1.** Provides a summary of the vaccines discussed. It is essential for pharmacists to continue to stay abreast of ongoing results of clinical trials with the vaccines currently in development.

**The Role of the Pharmacist in Managing Respiratory Syncytial Virus**

RSV has remained one of the leading causes of pediatric and adult morbidity and mortality worldwide, resulting in more deaths each year than influenza. Adequately managing and treating patients with RSV requires an interdisciplinary team to optimize care. Pharmacists are in a unique position to identify infants, children, and older adults with risk factors for RSV-associated lower respiratory tract infections (see TABLES 2 and 3).

Pharmacists can educate patients, parents, and caregivers on preventing transmission of RSV with proper handwashing, cough hygiene, avoiding close contact with infected individuals, and cleaning frequently touched surfaces. When patients receive an RSV diagnosis, pharmacists should educate the family that there are no pharmacologic treatments for RSV and supportive care and hydration are the mainstay of therapy. Pharmacists can ensure that patients have continuity of care from inpatient to outpatient settings. Providing communication with the interdisciplinary team will allow for the patient’s needs to be addressed, thereby minimizing the length of stay in the hospital. In the outpatient setting, pharmacists can advise with antibiotic stewardship concerning viral infection, discuss proper preventive measures, and recommend whether the patient may qualify for pharmacologic therapy with palivizumab. Pharmacists can also assist in the selection of appropriate nonprescription medications for symptom management. Connecting patients and families with essential resources (eg, CDC RSV surveillance, RSVprotection) to track current trends and RSV seasonality may help high-risk patients monitor RSV transmission in the community.

Pharmacists recognize that vaccination is the most effective strategy for preventing widespread diseases and their complications. Despite the barriers, there are several opportunities for RSV vaccine development to protect the most vulnerable populations. In addition, several lessons from previous vaccine attempts have helped design novel and informed effective strategies.
Disparities in care

An RSV vaccine’s main goal is to reduce disease severity, prevent post-RSV respiratory morbidity, and provide long-term immunity. Pharmacists must recognize patients at risk of severe RSV will benefit most from the RSV immunization once vaccines become available. Some studies indicate that besides some sociodemographic and environmental factors, including being a man, household crowding, and passive smoking, underlying medical conditions, such as prematurity, congenital heart disease, and chronic pulmonary and cardiovascular diseases, were associated with RSV disease. One study demonstrated risk factors for severe outcomes of RSV in patients 65 years and older included cystic fibrosis, neurological disorders, blood disease, liver disease, and renal failure.

Data related to racial disparities with RSV and older adults are lacking. In a study of Black and White children under 5 years of age who were hospitalized for acute respiratory illness found for RSV, rates were similar among Black and White children under 12 months of age but higher for Black children 12 months and older (for ages 12-23 months: RR 1.7; 95% CI, 1.1, 2.5; for ages 24-59 months: RR 2.2; 95% CI, 1.3, 3.6). The authors concluded that the racial disparities observed required further study. The National Medical Association has published a consensus panel paper titled, *Respiratory Syncytial Virus and African Americans.* Again, the emphasis is on children and not older adults. The paper does provide evidence that the areas with the longest duration of RSV disproportionately include higher percentages of African Americans. The longer duration of RSV season in these areas could impact both children and older adult incidence of RSV infection. A systematic review evaluating viral acute respiratory infections in the United States may provide additional information regarding racial and ethnic disparities in the future.

Patient education and increasing vaccination rates

Pharmacists can initiate conversations about RSV vaccination when patients present for other immunizations. Influenza and RSV seasons have significant overlap. Some of the RSV vaccine clinical trials have studied concomitant administration. Offering RSV vaccine in combination with influenza vaccine is a logical option. In addition, a complication of RSV can be lower respiratory tract infections, such as pneumonia. Offering the RSV vaccine in combination with the pneumococcal vaccine, again, is a logical option. Health Insurance Portability and Accountability Act-compliant marketing materials (eg, postcards and outbound automated phone calls) can be sent to high-risk older adults. In addition, pharmacists can offer RSV vaccination during comprehensive medication reviews as high-risk patients are identified. When the vaccine initially becomes available, many patients will be candidates, so hosting mass vaccination clinics may be beneficial. Once the early adopters have been vaccinated, RSV vaccine administration could be transitioned into the pharmacy workflow. Lessons learned from implementation and administration of COVID-19 vaccines can be applied to the RSV vaccine.

Vaccination rates vary by age, insurance status, urban or rural residence classification, and race/ethnicity. Vaccination rates among children are consistently high due to compulsory vaccination programs for school admittance. Adults do not necessarily have work vaccination requirements and therefore may not consider vaccination, resulting in lower vaccination rates. Barriers to adult immunization include lack of vaccine awareness, lack of recommendation from a health care provider, and the belief that healthy individuals do not need to be vaccinated. Nine solutions to address these barriers were presented in an article by Anderson. See Table 4 for a list of solutions.

Overall, vaccination coverage among non-Hispanic Black, Hispanic, and non-Hispanic Asian individuals has been lower than non-Hispanic White individuals. Multiple factors contribute to racial and ethnic differences in adult vaccination including differences in attitudes toward vaccination and preventive care, propensity to seek and accept vaccination, differences in quality of care received by racial and ethnic populations, and differences in concerns about vaccination. For example, in the 2017 to 2018 season, 49.3% of White

<table>
<thead>
<tr>
<th>TABLE 4. RECOMMENDATIONS FOR IMPROVING VACCINATION RATES AMONG ADULTS54</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patient education about risk factors for vaccine-preventable disease and availability of vaccines</td>
</tr>
<tr>
<td>• Public awareness campaigns promoting vaccines</td>
</tr>
<tr>
<td>• Access to vaccination services in convenient locations (eg, workplace, pharmacy)</td>
</tr>
<tr>
<td>• Reminder recall systems</td>
</tr>
<tr>
<td>• Standing order programs</td>
</tr>
<tr>
<td>• Audit vaccination rates</td>
</tr>
<tr>
<td>• Patient-specific recommendations from health care providers</td>
</tr>
<tr>
<td>• Vaccine assessment incorporated into clinical practice</td>
</tr>
<tr>
<td>• Train all staff to assess vaccination status of patients</td>
</tr>
</tbody>
</table>

54 For a list of solutions.
Adults 19 years or older, 39% of Black adults, and 37.5% of Hispanic adults received an influenza vaccine. This trend remains true for other vaccines, such as herpes zoster, pneumococcal, and tetanus. Pharmacists must be aware of these biases and viewpoints about vaccinations and educate patients on evidence-based facts.

Acceptance of a new vaccine is imperative to reduce morbidity and mortality of RSV, and potential barriers to vaccination must be addressed early. Mistrust regarding government institutions and programs, especially new ones, is an inherent problem, particularly in minority communities. That distrust has been built due to both structural and attitudinal reasons related to mishandling of public expectations and societal inequity. With RSV, there could be lower perceived risk of infection in older adults because RSV is typically thought of as an infection of pediatric patients. Pharmacists can use motivational interviewing strategies to identify patient concerns about RSV vaccination. Education can then be tailored to the patient to address those concerns. In addition, pharmacists can use local COVID-19 vaccine experiences to tailor their conversations to patients. Resources developed for COVID-19 will be applicable to RSV vaccines. Please visit: https://aspe.hhs.gov/pdf-report/vaccine-hesitancy for more information. Ultimately, it is the patient’s choice to be vaccinated and the pharmacist must respect that choice, but the pharmacist can tell the patient they will revisit this topic at a future visit. A patient-specific strong recommendation for vaccination from a healthcare provider is oftentimes all that is needed.

As a pharmacist, it is important to leverage consistent vaccine safety and efficacy messaging from government and public health agencies to promote RSV awareness and minimize the spread of misinformation. Transparency about the risk RSV poses along with potential vaccine adverse effects is essential to build trust. Failure to do so can create “vaccine opposition,” which can be highly difficult to overcome when combined with established feelings of mistrust. Building a rapport with the local community to share educational information will further establish trust in both the pharmacist and the vaccine to ensure higher vaccination rates.

Conclusion
RSV is a significant virus that infects infants, children, and older adults worldwide with a high rate of morbidity and mortality. Although symptoms are generally mild and cold-like, RSV can cause serious lower respiratory tract infections. Numerous vaccines are in various stages of development for RSV. Various vaccine platforms including live attenuated virus vaccines, subunit vaccines, vector-based vaccines, and nanoparticle vaccine approaches are being developed. Once a vaccine is FDA approved and recommended by the CDC, pharmacists and other members of the pharmacy team will have a critical role in ensuring appropriate distribution, administration, and monitoring of the RSV vaccine. Pharmacists will play a key role in identifying patients who are at high risk for RSV infection and complications, in addition to those who may be vaccine hesitant. Pharmacists can educate patients and their family members about the safety and efficacy of RSV vaccines.
REFERENCES


29. A phase III double-blind study to assess safety and efficacy of an RSV maternal unadjuvanted


POSTTEST QUESTIONS

1. Which patient is most likely presenting with symptoms of respiratory syncytial virus (RSV) infection?
   A. An 18-month-old boy with low-grade fever and tugging on the left ear
   B. A 14-year-old girl with intense pharyngitis and a temperature of 103 °F
   C. A 42-year-old man with sudden onset of extreme fatigue, myalgia, and cough
   D. A 70-year-old woman with gradual onset of nasal congestion, rhinorrhea, and cough for the past 4 days

2. Which patient is high risk for serious disease and complications from RSV infection?
   A. A 6-year-old girl attending kindergarten in the fall
   B. An 11-year-old boy presenting for the adolescent well visit
   C. A 34-year-old woman with isolated hypertension
   D. A 67-year-old man status post myocardial infarction

3. Which of the following RSV surface proteins is the most important target for vaccine development?
   A. G
   B. Prefusion F
   C. Postfusion F
   D. SH

4. Why was the original RSV vaccine candidate in the 1960s unsuccessful in clinical trials?
   A. Vaccinated RSV-exposed children, when exposed to natural RSV infection, had a higher incidence of acquiring RSV.
   B. Vaccinated RSV-naïve children experienced enhanced RSV disease when exposed to natural RSV infection.
   C. The vaccine did not meet prespecified efficacy criteria.
   D. Vaccinated mothers did not transfer antibodies to the infant prior to birth.

5. What is the mechanism of action for RSV vector-based vaccines?
   A. A nonreplicating modified version of a different virus serves as a carrier to deliver RSV proteins as an antigen to elicit an immune response.
   B. mRNA uses the host cell structures to produce the RSV fusion protein serving as an antigen to elicit an immune response.
   C. A weakened strain of RSV replicates in the nasal passages but not in the lungs to elicit an immune response.
   D. Multiple copies of modified RSV protein are combined into a single particle serving as an antigen to elicit an immune response.

6. Which manufacturer’s RSV vaccine currently in clinical trials uses an adenovirus vector to elicit the immune response?
   A. Bavarian Nordic
   B. Pfizer
   C. Novavax
   D. Janssen

7. An advantage of live attenuated RSV vaccines is that they can have which route of administration?
   A. Intradermal
   B. Intramuscular
   C. Intranasal
   D. Subcutaneous

8. Which of the following vaccine candidates is being evaluated in a phase 3 maternal immunization trial to prevent RSV infection in infants during the first few months of life?
   A. GSK3888550A
   B. ResVax
   C. ChAd155-RSV
   D. RSVpreF
POSTTEST QUESTIONS (continued)

9. Which of the following is an important consideration that pharmacists should be aware of when identifying adults to educate about RSV and emerging vaccines?
   A. Vaccination rates among children and adults are consistently high due to compulsory school/work requirements.
   B. Vaccination coverage among non-Hispanic Asian individuals is higher than non-Hispanic White individuals.
   C. Being a man, household crowding, and passive smoking were associated with RSV disease.
   D. RSV vaccines should be separated from the administration of the annual influenza vaccine.

10. Which of the following is a role of the pharmacist in managing RSV infection?
   A. Recommend use of palivizumab for all infants during RSV season.
   B. Recommend use of antibiotics for the treatment of RSV infection.
   C. Recommend oral ribavirin for hospitalized patients who are RSV-positive as part of antibiotic stewardship.
   D. Educate patients about over-the-counter supportive therapy for RSV.

INSTRUCTIONS FOR EARNING CREDIT

Begin the activity by reading the content in its entirety.
Go to www.pharmacytimes.org/go/RSV to access the online version of this activity.
Click “Proceed,” then complete the online pretest.
Once completed, click “Next” until reaching the activity posttest.
Complete the online posttest and activity evaluation form.
After successfully completing the posttest and evaluation form, this information will be uploaded to CPE Monitor.
You must complete these steps before the activity expires in order to receive your credit.
You may view your credit within 48 hours at www.mycpemonitor.net

NOTE: Your CE credit will be automatically uploaded to CPE Monitor. Please ensure that your Pharmacy Times® account is updated with your NABP e-profile ID number and your date of birth. Participation data will not be uploaded into CPE Monitor if you do not have your NABP e-profile ID number and date of birth entered into your profile on www.pharmacytimes.org.

SYSTEM REQUIREMENTS FOR COMPLETION:
Computer or smartphone with internet-access web browser (IE7.0+ or Webkit-/Mozilla-compatible) with JavaScript enabled.

FOR QUESTIONS ABOUT THIS INTERNET CPE ACTIVITY, PLEASE CONTACT: ceinfo@pharmacytimes.com.
PRIVACY POLICY AND TERMS OF USE INFORMATION: www.pharmacytimes.org/terms.

EDUCATIONAL DISCLAIMER: Continuing professional education (CPE) activities sponsored by Pharmacy Times Continuing Education™ are offered solely for educational purposes and do not constitute any form of professional advice or referral. Discussions concerning drugs, dosages, and procedures may reflect the clinical experience of the author(s) or they may be derived from the professional literature or other sources and may suggest uses that are investigational in nature and not approved labeling or indications. Participants are encouraged to refer to primary references or full prescribing information resources.
Advancing Treatment of Chronic Kidney Disease in Patients With Diabetes: Key Considerations for Pharmacists

**FACULTY**
Joshua J. Neumiller, PharmD, CDCES, FADCES, FASCP  
Vice-Chair & Allen I. White Distinguished Professor  
Department of Pharmacotherapy  
College of Pharmacy and Pharmaceutical Sciences  
Washington State University  
Spokane, Washington

**DISCLOSURES**
The following contributor has relevant financial relationships with commercial interests to disclose:

**FACULTY**
Joshua J. Neumiller, PharmD, CDCES, FADCES, FASCP  
Consultant: Novo Nordisk  
Speakers Bureau: Dexcom

The following contributors have no relevant financial relationships with commercial interests to disclose:

**PHARMACY TIMES CONTINUING EDUCATION™ PLANNING STAFF**
Jim Palatine, RPh, MBA; Maryjo Dixon, RPh; Michelle C. Carlson, PharmD; Kylie Ferrentino; Susan Pordon; Brianna Winters; and Chloe Taccetta

**PHARMACY TIMES® EDITORIAL STAFF**
Davy James

Anonymous peer reviewers were part of the content validation and conflict resolution and have no financial relationships with commercial interests to disclose.

**INTRODUCTION**
The number of persons living with diabetes continues to increase in the United States. An estimated 34.2 million Americans currently have diabetes, according to most recent estimates from the Centers for Disease Control and Prevention (CDC). The majority (90%-95%) of individuals have type 2 diabetes (T2D), with type 1 diabetes (T1D) accounting for 5% to 10% of the overall diabetes population. A primary goal of management for patients with diabetes is the prevention and/or delay of diabetes-related complications. While it is clearly important to manage blood glucose to avoid symptoms and complications of hyperglycemia (eg, frequent urination, thirst, blurred vision, fatigue, increased infection risk), optimization of blood glucose control can also reduce risk of onset and progression of microvascular complications such as kidney disease, retinopathy, and neuropathy. Similarly, cardiovascular (CV) risk reduction is important in people with diabetes to reduce the risk for microvascular and macrovascular (eg, myocardial infarction, stroke) complications. Fortunately, many significant advancements in the management of diabetes have surfaced over the past several years, including new technologies and new and emerging pharmacologic therapies to improve glucose control and mitigate CV and kidney risk. This article will focus on recent guidance and emerging therapies to improve kidney outcomes in patients with T2D and chronic kidney disease (CKD), and discuss the important role pharmacists can play in optimizing care for this high-risk population.

**EDUCATIONAL OBJECTIVES**
At the completion of this activity, the participant will be able to:

- Identify the epidemiology of diabetes and chronic kidney disease (CKD) as well as the pathology of kidney disease in this patient population and the impact of inflammation and fibrosis as a progressive factor
- Analyze current guidelines for CKD and type 2 diabetes (T2D) and the clinical trial data surrounding the emerging nonsteroidal mineralocorticoid receptor antagonists in treatment
- Illustrate the impact of pharmacists in coordination of care and treatment strategies for CKD in patients with T2D

**TARGET AUDIENCE:** Pharmacists

**ACTIVITY TYPE:** Application

**RELEASE DATE:** July 30, 2021

**EXPIRATION DATE:** August 31, 2022

**ESTIMATED TIME TO COMPLETE ACTIVITY:** 2.0 hours

**FEE:** This lesson is offered for free at www.pharmacytimes.org.

Pharmacy Times Continuing Education™ is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education. This activity is approved for 2.0 contact hours (0.20 CEU) under the ACPE universal activity number 0290-0000-21-284-H01-P. The activity is available for CE credit through August 31, 2022.
Diabetes and CKD: Diagnosis and Classification, Epidemiology, and Pathophysiology

**Diagnosis and Classification of CKD**

CKD is defined by the presence of persistently reduced estimated glomerular filtration rate (eGFR <60 mL/min/1.73m²), persistently elevated urine albumin excretion (≥30 mg/gram creatinine), or both, for greater than 3 months. The American Diabetes Association (ADA) recommends urinary albumin and eGFR screening in all patients with T2D at least annually. More frequent monitoring is recommended for patients with a history of severely increased albuminuria (urinary albumin-to-creatinine ratio [UACR] >300 mg/gram creatinine) and/or an eGFR of 30 to 60 mL/min/1.73m².

**FIGURE 1** provides a visual “heat map” summary of CKD prognosis as stratified by GFR and albuminuria categories. As illustrated in the figure, lower eGFR and higher levels of albuminuria are associated with greater relative risks for CKD progression and poor clinical outcomes (e.g., acute kidney injury, progression to kidney failure, and mortality).

Kidney disease attributable to diabetes is often referred to as diabetic kidney disease (DKD). While CKD occurring in patients with T2D is usually attributable to diabetes, patients with diabetes can present with other etiologies of kidney disease. Considering the heterogeneity in CKD etiology that exists for patients with T2D, current clinical practice recommendations promote treating most presentations of T2D and CKD similarly, with the patient-centered treatment approach informed by the patient’s eGFR and albuminuria category.

In this article, the terms “CKD in T2D” and “DKD” will be used interchangeably.
Epidemiology and Disease Burden

An estimated 37 million adults in the United States have CKD, with most remaining undiagnosed. Overall, kidney diseases are ranked as the ninth leading cause of death in the United States, with diabetes and hypertension responsible for approximately 75% of new cases of kidney failure. DKD occurs in approximately 40% of patients with T2D, and is a major contributor to morbidity and mortality. Besides the impending risk for progression to kidney failure, patients with DKD are at high risk for experiencing CV events, cerebrovascular events, infections, hospitalizations, and death. Unfortunately, the prevalence of DKD has increased in recent years in parallel with the increased prevalence of diabetes. While large improvements in morbidity and mortality attributed to other diabetes-related complications (eg, myocardial infarction, stroke, limb amputation) have been observed, temporal improvements in DKD outcomes such as progression to kidney failure and occurrence of kidney-related death are less robust. Interventions to improve outcomes in patients with T2D and CKD, including novel therapeutics and management strategies, are drastically needed.

Pathophysiology of DKD

The pathophysiology of DKD is complex and involves multiple interrelated etiologic pathways and factors. A combination of metabolic, hemodynamic, inflammatory, and fibrotic changes occur in the diabetic state that, in turn, contribute to structural and functional abnormalities characteristic of DKD (see FIGURE 2). Hyperglycemia itself drives the production of advanced glycation end products (AGE) and accumulation of reactive oxygen species that promote cellular injury. Glomerular hyperfiltration, contributed to by systemic hypertension and obesity, occurs in up to 40% of patients with T2D and has long been associated with development and progression of CKD. Renin-angiotensin system (RAS) inhibitors (angiotensin-converting enzyme [ACE] inhibitors and angiotensin receptor blockers [ARBs]) were the first medications approved for the treatment of DKD and directly target glomerular hyperfiltration. Pathophysiologic overactivation of the mineralocorticoid receptor has also been implicated in the pathophysiology of DKD through promotion of inflammation and fibrosis, with mineralocorticoid receptor blockade under active investigation as an approach to slow kidney disease progression. Novel nonsteroidal mineralocorticoid receptor antagonists (MRAs) are discussed later in detail. While core to the pathophysiology of DKD, these pathophysiologic factors are also deleterious to the CV system. Indeed, patients with DKD are at increased risk for CV disease-related morbidity and mortality, and management of CV disease risk factors is considered a cornerstone of comprehensive care in patients with T2D and CKD. The term cardio-renal syndrome (CRS) has been coined to describe how overlapping organ dysfunction often occurs in the kidney and heart.

Current and Emerging Treatment Options for Patients With T2D and CKD

The treatment of CKD in T2D involves a multifaceted approach targeting modifiable risk factors for kidney and CV diseases. FIGURE 3 provides a framework for kidney and heart risk management in patients with T2D and CKD.
factor management, as recommended within the KDIGO 2020 Clinical Practice Guideline for Diabetes Management in CKD. As illustrated in the figure, KDIGO recommends optimization of guideline-directed medical therapy inclusive of lifestyle intensification (nutrition management and physical activity), blood pressure control, glycemic control, lipid management with a statin, smoking cessation, and antplatelet therapy when applicable and indicated. In addition to risk factor management, recent data on the use of select glucose-lowering therapies (eg, sodium-glucose cotransporter-2 [SGLT2] inhibitors, glucagon-like peptide-1 receptor agonists [GLP-1 RAs]), and nonsteroidal MRAs to mitigate kidney and CV risk are transforming the landscape of CKD management. Additional information on key current and emerging treatment options for patients with T2D and CKD are detailed below.

**Lifestyle Interventions**

As highlighted in **FIGURE 3**, lifestyle interventions including implementation of healthy eating patterns and engaging in physical activity are recommended for all patients with T2D and CKD. Healthy lifestyle can directly address the 2 salient modifiable risk factors for development and progression of DKD: hyperglycemia and hypertension. Key nutritional considerations include adoption of a generally healthy and balanced diet, maintaining appropriate protein intake, and avoiding excessive sodium consumption. Like other patients with diabetes, those with DKD benefit from individualized diets that stress consumption of whole foods such as vegetables, fruits, whole grains, fiber, legumes, plant-based proteins, unsaturated fats, and nuts. Limited consumption of processed meats, refined carbohydrates, and sweetened beverages is encouraged. While dietary protein restriction has been proposed as a strategy to slow DKD progression, KDIGO recommends following the World Health Organization (WHO) recommended daily allowance for protein intake of 0.8 gram/kg per day with an emphasis on plant-based sources for patients with DKD. In the setting of dialysis, a higher daily protein intake of 1.0 to 1.2 grams/kg per day is recommended. It is additionally recommended that patients with T2D and CKD limit dietary sodium intake to less than 2 grams per day. Adherence to clinical nutritional guidance and recommendations is low in patients with CKD. Therefore, engaging patients in the development of an individualized nutrition plan is critical to promote healthy behavior change and implement an eating plan that is feasible given patient-specific considerations (eg, cultural considerations, food intolerance, resources).

Patients with T2D and CKD overall engage in lower levels of physical activity when compared with the rest of the population. Because lower levels of physical activity and fitness are associated with both CV events and mortality, encouraging appropriate physical activity in patients with T2D and CKD is an important component of their overall care. KDIGO recommends that patients with T2D and CKD engage in moderate-intensity physical activity at least 150 minutes per week, or at a level appropriate given their CV and physical tolerance. Recommendations for physical activity should be individualized and consider age, relevant comorbidities, access to resources, and other relevant barriers.

**Glucose Control**

Optimization of glucose control to slow the onset and/or progression of CKD is considered a cornerstone of DKD management. Targeting lower hemoglobin A1c (A1C) values through intensifying glucose control reduces risk for the development of diabetes-related complications in both T1D and T2D. Focusing on patients with T2D, the landmark trial supporting early intensive glucose control is the United Kingdom Prospective Diabetes Study (UKPDS). While between-group differences in glycemic control were lost 1 year into the post-trial follow-up stage of the UKPDS, 10 to 12 years of post-trial follow-up showed a 24% reduction in risk of microvascular complications, including macroalbuminuria, as well as a reduc-
in the rate of serum creatinine doubling in the intensive compared with conventional therapy group (0.9% vs 3.5%; \( P = .0028 \)).30,31 This “metabolic memory” achieved from early intensive glycemic control in patients with T2D highlights the importance of glucose control early in the natural history of T2D to mitigate kidney risk. Currently the ADA recommends a general A1C target of lower than 7.0% for most nonpregnant adults with diabetes, although it is stressed that individualized glycemic targets be made in consideration of patient-specific factors including risk of adverse effects (AEs) (eg, hypoglycemia) and the presence of important comorbidities.32

In patients with DKD, achieving individualized glycemic targets can be complicated by a reduced capacity for gluconeogenesis in the kidney and impaired clearance of glucose-lowering therapies.5,33 Combined, these factors place patients with DKD at high risk for experiencing hypoglycemia or other AEs. Balancing risks of treatment with the importance of optimized glucose control, KDIGO recommends an A1C target ranging from less than 6.5% to less than 8.0%. KDIGO recommends setting an individualized A1C target within this range in consideration of CKD severity, comorbidities, life expectancy, and hypoglycemia risk (propensity for treatment to cause hypoglycemia, resources for hypoglycemia management, and presence of hypoglycemia unawareness).4 In terms of glucose-lowering therapy recommendations, KDIGO recommends a combination of metformin plus an SGLT2 inhibitor as first-line pharmacotherapy in most patients with T2D and CKD who have an eGFR greater than or equal to 30 mL/min/1.73m².4 Additional glucose-lowering agents are then added as necessary to achieve patient-specific glycemic targets, with preference given to the addition of a long-acting GLP-1 RA.4

Both ADA and KDIGO preferentially recommend agents with proven CKD benefit from the SGLT2 inhibitor and GLP-1 RA medication classes.3,5,21,34 These recommendations from ADA and KDIGO largely align with guidance from other organizations including the American College of Cardiology (ACC), the American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE), and the joint consensus developed by the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD).35,37 Evidence supporting the most recent recommendations from the ADA and KDIGO are discussed below for each class respectively.

SGLT2 Inhibitors
In addition to improving metabolic control through reductions in glycemia, body weight, and blood pressure, SGLT2 inhibitors are believed to provide kidney protective effects by reducing glomerular hyperfiltration.38,39 SGLT2 inhibitors currently available in the United States include canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin.34 The initial clinical signal for kidney benefit with SGLT2 inhibitors came from secondary outcomes reported in the CV outcome trials (CVOTs) conducted with canagliflozin, dapagliflozin, and empagliflozin, with all trials demonstrating slowed DKD onset and progression with SGLT2 inhibition.40-41 Subsequently, dedicated kidney outcome trials were conducted to specifically test the effects of SGLT2 inhibitors on CKD progression. The Canagliflozin and Renal Events Reduction in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial enrolled participants with eGFR greater than or equal to 30 and less than 90 mL/min/1.73m² and severely increased albuminuria.42 After a mean follow-up period of 2.6 years, the composite outcome inclusive of end-stage renal disease (ESRD), doubling of serum creatinine, or death from kidney disease causes was lower in the canagliflozin group (hazard ratio [HR], 0.66; 95% confidence interval [CI], 0.53-0.81; \( P < .001 \)). Canagliflozin treatment also improved CV and heart failure (HF) outcomes, which are common comorbidities and contributors to morbidity and mortality in CKD.44 The Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) was the second SGLT2 inhibitor kidney outcome trial published.45 DAPA-CKD enrolled patients with CKD with an eGFR greater than or equal to 25 and less than or equal to 75 mL/min/1.73m² and a UACR greater than or equal to 200 and less than or equal to 5000 mg/gram.45 The primary composite outcome of a sustained decline in eGFR of greater than or equal to 50%, ESRD, or death from CV or kidney disease was significantly reduced with dapagliflozin treatment (HR, 0.61; 95% CI, 0.51-0.72; \( P < .001 \)).45 Notably, the benefit of SGLT2 inhibitor treatment observed in both trials was on top of background-optimized treatment with an ACE inhibitor or an ARB. A kidney outcome study with empagliflozin, the Study of Heart and Kidney Protection with Empagliflozin (EMPA-KIDNEY), is currently in progress.46

GLP-1 RAs
There is increasing evidence that GLP-1 RA therapy also provides kidney benefit. There are currently 7 GLP-1 RA products commercially available in the United States: dula-
glutide, exenatide, exenatide extended-release, liraglutide, lixisenatide, injectable semaglutide, and oral semaglutide. Secondary kidney outcomes from multiple CVOTs have reported benefits on albuminuria onset and progression, and a clinical trial with dulaglutide reported benefits on eGFR decline with dulaglutide treatment when compared with insulin glargine. A meta-analysis of GLP-1 RA CVOTs evaluated a composite kidney outcome inclusive of development of severely increased albuminuria, decline in eGFR or increase in creatinine, progression to kidney failure, or death due to kidney disease. The analysis found GLP-1 RA treatment was associated with a 17% relative risk reduction in the composite outcome (HR, 0.83; 95% CI, 0.78-0.89; P <.001). While kidney disease outcome data with GLP-1 RAs are currently limited to secondary outcomes and analyses, the Effect of Semaglutide Versus Placebo on the Progression of Renal Impairment in Subjects With Type 2 Diabetes and Chronic Kidney Disease (FLOW) study is testing the impact of injectable semaglutide on a primary kidney composite outcome (≥50% eGFR decline, kidney failure, and death from kidney disease or CV disease) in patients with DKD. As previously discussed, KDIGO currently preferentially recommends a long-acting GLP-1 RA in patients with T2D and CKD if they require additional glucose lowering beyond first-line combination therapy with metformin plus an SGLT2 inhibitor. Considering the high risk of hypoglycemia in patients with CKD, GLP-1 RAs offer a safe and effective alternative to insulin, especially in patients with advanced CKD, with evidence supporting their use down to an eGFR of 15 mL/min/1.73m². 

Blood Pressure Control
Elevated blood pressure is tightly associated with negative kidney and CV outcomes in patients with CKD; thus, blood pressure management is a critical component of comprehensive CKD care. The UKPDS reported in the 1990s that targeting a blood pressure of lower than 150/85 mm Hg versus a target of lower than 180/105 mm Hg resulted in significant risk reductions for microvascular complications. KDIGO suggests that adults with CKD and hypertension be treated to a target systolic blood pressure of lower than 120 mm Hg when appropriate and tolerated. Clinical practice guidelines consistently recommend treatment with an ACE inhibitor or an ARB in patients with diabetes, hypertension, and albuminuria at the highest tolerated dose approved for use. Additional antihypertensive medications (eg, thiazide diuretics, dihydropyridine calcium channel blockers) are then added to meet individualized blood pressure targets. Dual RAS blockade (eg, ACE inhibitor plus an ARB), however, is not recommended. Unfortunately, despite consistent recommendations for use in the setting of DKD, RAS inhibitor therapy is widely underutilized in patients with CKD.

Use of steroidal MRAs, such as spironolactone and eplerenone, have been shown in small studies to decrease blood pressure in cases of resistant hypertension and to lower albuminuria in patients with diabetes with elevated urinary albumin excretion. On the background of ACE inhibitor or ARB therapy, however, the use of steroidal MRAs carries increased risk for hyperkalemia and acute reductions in eGFR. Use of steroidal MRAs in routine clinical practice is limited in the setting of T2D and CKD. Newer nonsteroidal MRAs, however, have shown promise in improving outcomes in patients with T2D and CKD with improved tolerability. Nonsteroidal MRAs are discussed in additional detail in the following section.

Emerging Therapies in T2D and CKD: Focus on Nonsteroidal MRAs
Despite the current standard of care, including the recent introduction of SGLT2 inhibitors and GLP-1 RAs to slow DKD progression, there remains residual risk for development and progression of CKD in patients with T2D. To address this residual risk, novel therapies targeting the key pathophysiologic drivers of DKD are needed to improve kidney outcomes. Two novel therapeutic classes that have shown promise in the setting of DKD include selective endothelin receptor antagonists (ERAs) and nonsteroidal MRAs. This section will focus on the novel nonsteroidal MRAs. As previously discussed, overactivation of the mineralocorticoid receptor (MR) has been identified as a key driver of inflammation and fibrosis in both the kidney and heart. FIGURE 4 highlights key drivers of DKD progression and therapeutics targeting each. As noted previously, traditional steroidal MRA use is limited in the setting of T2D and CKD due to concerns regarding risks of hyperkalemia, GFR decline, and antiandrogenic AEs such as gynecomastia. Current evidence with nonsteroidal MRAs, including finerenone and elexarenone, suggest benefit of these agents in patients with T2D and CKD with more favorable safety and tolerability profiles.

Finerenone
Finerenone is a novel nonsteroidal MRA that has been shown in vitro to have greater receptor selectivity when compared
with spironolactone and eplerenone, and is at least as potent as spironolactone.\(^{59,64}\) Finerenone binds the MR in a unique fashion and acts as a bulky, passive antagonist.\(^{59}\) This unique mechanism of MR binding differentiates finerenone from spironolactone and eplerenone. Its unique binding to the MR combined with the unique physicochemical properties of finerenone likely account for its differential clinical response when compared with steroidal MRAs.\(^{59}\) Multiple phase 2 and phase 3 trials have been completed with finerenone. The \(\text{TABLE}\)^{60,65-67} provides a summary of key finerenone clinical trial findings to date. Finerenone was approved by the FDA in July 2021 to reduce the risk of sustained eGFR decline, ESRD, CV death, nonfatal myocardial infarction, and hospitalization for HF in adults with CKD associated with T2D.\(^{68}\) Clinical trial evidence supporting the approval of finerenone is briefly reviewed below.

The phase 2 ARTS (Mineralocorticoid Receptor antagonist Tolerability Study) program included a variety of participants with elements of cardiorenal syndrome.\(^{55,67}\) The ARTS study showed that finerenone was equally effective in lowering albuminuria and cardiac markers of hemodynamic stress when compared with spironolactone, with smaller increases in hyperkalemia in patients with HF with reduced ejection fraction (HFrEF) and CKD.\(^{65}\) Notably, the incidence of events related to worsening of kidney function was lower with finerenone when compared with spironolactone in the ARTS trial.\(^{65}\) ARTS-Heart Failure (ARTS-HF) was another study that enrolled participants within 7 days of hospital treatment for worsening chronic HFrEF who had comorbid T2D and/or CKD.\(^{66}\) Participants received either finerenone or eplerenone for 90 days. Reduction in N-terminal pro-B-type natriuretic peptide (NT-proBNP) was similar between the finerenone and eplerenone groups. Numerically fewer participants receiving finerenone, however, experienced the composite outcome inclusive of death from any cause, CV hospitalization, or emergency treatment for worsening HF. ARTS-Diabetic Nephropathy (ARTS-DN) enrolled 823 participants with T2D and CKD receiving stable background therapy with an ACE inhibitor or ARB.\(^{67}\) ARTS-DN tested the safety and efficacy of finerenone versus placebo over 90 days of treatment. Finerenone treatment was associated with a dose-dependent reduction in UACR, with no differences in the incidence of an eGFR decline of 30% from baseline. Discontinuation rates due to hyperkalemia were low and ranged from 0% to 3.2% in the finerenone treatment arms.

Based on positive findings from the ARTS program, several phase 3 clinical trials are completed or underway with finerenone in patients with components of the cardiorenal syndrome.\(^{59,65,70}\) The Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes (FIDELIO-DKD) trial studied finerenone in 5734 participants with T2D and CKD (eGFR ≥25 to <75 mL/min/1.73m\(^2\)) and a UACR ≥300 to ≤5000 mg/gram or eGFR ≥25 to <60 mL/min/1.73m\(^2\) and a UACR ≥30 to <300 mg/gram with retinopathy).\(^{66}\) Compared with placebo, finerenone reduced risk of the composite primary kidney disease outcome (kidney failure, a sustained decrease in eGFR of ≥40% or death from kidney disease) by 18% (HR, 0.82; 95% CI, 0.73-0.93; \(P = .001\)). The key secondary composite outcome (death from CV causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for HF) was also reduced (HR, 0.86; 95% CI, 0.75-0.99; \(P = .03\)). While the incidence of hyperkalemia-related study discontinuation was higher with finerenone compared with placebo, event rates were low (2.3% vs 0.9%, respectively).\(^{46}\) Preliminary results from the Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD) trial indicate that finerenone treatment successfully reduced the composite primary end point of time to first occurrence of CV death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for HF.\(^{69,71}\)
### Table: Key Clinical Trial Findings with Finerenone

<table>
<thead>
<tr>
<th>Trial (N)</th>
<th>ARTS (N=65 in part A; N=392 in part B)</th>
<th>ARTS-HF (N=1066)</th>
<th>ARTS-DN (N=823)</th>
<th>FIDELIO-DKD (N=5734)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Key inclusion criteria</strong></td>
<td>• HFref (LVEF ≤40%)</td>
<td>• Worsening chronic HFref (LVEF ≤40%) requiring hospitalization and treatment with IV diuretics</td>
<td>• T2D and CKD</td>
<td>• T2D and CKD</td>
</tr>
<tr>
<td></td>
<td>• CKD</td>
<td>• T2D and/or CKD</td>
<td>• UACR ≥30 mg/gram, eGFR &gt;30</td>
<td>• UACR ≥30 to &lt;300 mg/gram, eGFR ≥25 to &lt;75</td>
</tr>
<tr>
<td></td>
<td>• eGFR 60-90 (part A)</td>
<td>• eGFR &gt;30 in patients with T2D</td>
<td>• eGFR &gt;30</td>
<td>or ( eGFR \geq 25 ) to &lt;75</td>
</tr>
<tr>
<td></td>
<td>• eGFR 30-60 (part B)</td>
<td>• eGFR 30-60 in patients without T2D</td>
<td>• Receiving RAS blocker</td>
<td>( eGFR \geq 25 ) to &lt;75</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Part A</td>
<td>• Finerenone 2.5, 5, or 10 mg once daily</td>
<td>• Finerenone 2.5-15 mg daily, up-titrated to 5-20 mg on day 30</td>
<td>• Finerenone 1.25-25 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Placebo</td>
<td>• Eplerenone 25 mg every other day, up-titrated to 25 mg daily on day 30 and to 50 mg daily on day 60</td>
<td>• Placebo</td>
</tr>
<tr>
<td></td>
<td>Part B</td>
<td>• Finerenone 2.5, 5, or 10 mg once daily, or 5 mg twice daily</td>
<td>• Spironolactone 25-50 mg per day</td>
<td>• Finerenone 10-20 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Placebo</td>
<td>• Placebo</td>
<td>• Placebo</td>
</tr>
<tr>
<td><strong>Key outcomes</strong></td>
<td>Part A</td>
<td>• Safety and tolerability of finerenone vs placebo</td>
<td>• &gt;30% decrease in NT-proBNP</td>
<td>• Composite of kidney failure, sustained decrease of ≥40% in eGFR, or death from renal causes (primary)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Change in serum potassium with finerenone vs placebo and open-label spironolactone</td>
<td>• Composite of death from any cause, CV hospitalization, or emergency presentation for worsening chronic HF</td>
<td>• Composite of CV death, nonfatal MI, nonfatal stroke, or hospitalization for HF (secondary)</td>
</tr>
<tr>
<td></td>
<td>Part B</td>
<td>• Change in serum potassium with finerenone vs placebo and open-label spironolactone</td>
<td>• Occurrence of hyperkalemia leading to study discontinuation</td>
<td>• Occurrence of hyperkalemia leading to study discontinuation</td>
</tr>
<tr>
<td><strong>Treatment duration</strong></td>
<td>28 days</td>
<td>90 days</td>
<td>90 days</td>
<td>2.6 years (median duration of follow-up)</td>
</tr>
</tbody>
</table>

**Key findings**

• Finerenone treatment associated with smaller increases in serum potassium and lower incidence of hyperkalemia when compared with spironolactone
• Finerenone was equally effective in lowering albuminuria and cardiac biomarkers when compared with spironolactone
• The proportion of patients experiencing >30% decrease in NT-proBNP was similar with finerenone and eplerenone
• Incidence of the composite outcome occurred numerically less frequently with finerenone vs eplerenone
• Finerenone treatment resulted in a dose-dependent reduction in UACR
• No participants in the finerenone 10 mg per day group discontinued due to hyperkalemia; discontinuation rates due to hyperkalemia in the finerenone 7.5, 15, and 20 mg per day groups were low (1.7-3.2%)
• Both composite outcomes were significant for finerenone versus placebo

**ARTS**: Mineralocorticoid Receptor Antagonist Tolerability Study; **ARTS-DN**: ARTS-Diabetic Nephropathy; **ARTS-HF**: ARTS-Heart Failure; **CKD**: chronic kidney disease; **CV**: cardiovascular; **eGFR**: estimated glomerular filtration rate; **FIDELIO-DKD**: Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes; **HF**: heart failure; **HFrEF**: heart failure with reduced ejection fraction; **HR**: hazard ratio; **IV**: intravenous; **LVEF**: left ventricular ejection fraction; **MI**: myocardial infarction; **NT-proBNP**: N-terminal pro-B-type natriuretic peptide; **RAS**: renin-angiotensin system; **T2D**: type 2 diabetes; **UACR**: urinary albumin-to-creatinine ratio.
Esaxerenone

Esaxerenone, another nonsteroidal MRA that has been studied for the treatment of hypertension and CKD, is currently approved for use in Japan to treat essential hypertension. Esaxerenone with Placebo in Japanese Type 2 Diabetic Patients with Microalbuminuria (ESAX-DN) was a randomized, double-blind, placebo-controlled trial conducted in 455 participants with T2D and a UACR of 45 to less than 300 mg/gram. Participants were treated with background RAS inhibitor therapy. The primary end point was the proportion of patients achieving UACR remission, defined as UACR less than 30 mg/gram creatinine and a greater than or equal to 30% reduction in UACR from baseline at 2 consecutive time points after treatment. Findings showed that 22% of participants compared with 4% in the esaxerenone and placebo groups, respectively, achieved the primary end point (P < .001). The percent change in UACR from baseline to end of study was ~58% for the esaxerenone arm compared with an increase of 8% for the placebo group. More patients receiving esaxerenone had measured serum potassium levels greater than or equal to 5.5 mEq/L on 2 consecutive measurements when compared with those receiving placebo, but the investigators reported these events were asymptomatic and resolved following esaxerenone dose reduction or treatment discontinuation.

Together, these positive findings with finerenone and esaxerenone provide strong support for use of these agents in patients with cardio renal syndrome. As finerenone has been recently approved by the FDA, it is anticipated that guideline forming groups will quickly recommend finerenone use to improve CKD outcomes in appropriate patients.

STAR
How can pharmacists help improve CKD outcomes for patients with T2D?

The Role of the Pharmacist in Improving CKD Outcomes

As medication experts, pharmacists can play an important role in the multidisciplinary care team to overcome barriers and increase utilization of evidence-based therapies in patients with T2D and CKD. Patients with T2D and CKD represent a particular management challenge as multiple providers (eg, diabetologists, cardiologists, nephrologists) are often involved in their care, sometimes resulting in gaps in communication and development of medication-related problems. Further complicating patient management, patients with CKD are frequently managed with multiple medications from a variety of medication classes, thus increasing the risk for AEs and clinically important drug interactions. Medication regimen adherence is another important consideration, with medication nonadherence in patients with multiple chronic medical conditions potentially contributing to increased costs, hospitalizations, AEs, and worsening disease progression. As critical members of the health care team, pharmacists can address communication gaps between providers and patients to optimize medication use and outcomes. Pharmacists can facilitate medication reconciliation and address issues related to therapeutic duplication and/or drug interactions. Additionally, educating the patient and/or their caregiver about the importance of adhering to recommended therapies and lifestyle recommendations is an important role pharmacists can play to improve CKD outcomes in patients with T2D. While large robust clinical trials examining outcomes from pharmacist-centered interventions are lacking, current evidence supports that pharmacist interventions generally have a positive impact on clinical, economic, and humanistic outcomes.

Multidisciplinary CKD care models have been reported to delay CKD progression as well as decrease hospitalization rates, reduce CV events, and lower all-cause mortality. The National Kidney Foundation (NKF) supports the development of multidisciplinary teams to define organizational CKD treatment strategies, and encourages integration of clinical pharmacists into the care path for management of hypertension and CKD, with evidence supporting the benefit of pharmacist co-management to improve blood pressure control in patients with T2D and CKD. In line with these recommendations from NKF, pharmacists are clearly well suited to assist with care coordination and/or contribute to many of the stated core functions of the team-based approach to CKD care proposed by KDIGO. Specific activities where pharmacists can impact care may include review of treatment targets and adjustment of pharmacotherapeutic agents (eg, SGLT2 inhibitors, ACE inhibitors/ARBs, statins), assessment of kidney function and cardiometabolic risk factors (eg, blood pressure, body weight, A1C), and provision of self-management education. Leveraging clinical pharmacists within multidisciplinary care teams could address several barriers to optimal care in patients with DKD, including addressing time constraints that limit primary care providers and specialists, provision of patient-centered disease state and medication education, frequent review of the medication regimen to assess for inappropriate use of nephrotoxins (eg,
nonsteroidal anti-inflammatory drugs, proton pump inhibitors), and adherence to evidence-based DKD care (use of ACE inhibitors/ARBs and SGLT2 inhibitors) in close collaboration with other members of the care team.

As previously mentioned, patients with T2D and CKD require careful follow-up to ensure appropriate medication management. Reinforcement of medication-specific counseling is important to optimize adherence and safety. An important aspect of patient education is teaching effective risk mitigation strategies for safe medication use. For SGLT2 inhibitors, this includes hygiene counseling to avoid genital mycotic infections, provision of sick day rules and insulin administration guidelines to reduce risk of SGLT2 inhibitor-associated ketoacidosis, and best practices for foot self-care. SIMILARLY, FOR GLP-1 RAS, PATIENTS WITH T2D AND CKD SHOULDN’T BE INITIATED ON A LOW DOSE AND TITRATED UPWARD SLOWLY TO MINIMIZE THE RISK OF GASTROINTESTINAL AEs SUCH AS NAUSEA AND VOMITING. WHEN STARTING AN SGLT2 INHIBITOR OR GLP-1 RA IN A PATIENT ON BACKGROUND INSULIN AND/OR SUFONYLUREA THERAPY, THE BACKGROUND INSULIN AND/OR SUFONYLUREA AGENTS MAY NEED TO BE REDUCED TO MINIMIZE THE RISK OF HYPOGLYCEMIA. A SMALL PILOT STUDY (N = 14) DEMONSTRATED THE FEASIBILITY OF A PHARMACIST-NPHEEOLOGIST COLLABORATION TO MANAGE SGLT2 INHIBITOR USE.

Pharmacists were embedded within a multidisciplinary nephrology clinic and aided in SGLT2 inhibitor initiation and monitoring through providing patient education, telephone follow-up, and care coordination. Following SGLT2 inhibitor initiation, the pharmacists frequently followed up with patients to ensure safety, which included titration of concomitant medications for diabetes and hypertension. Overall, UACR (mean change of −12% ± 61%) improved, with the co-management strategy allowing pharmacists to facilitate intensive follow-up that may be overly time intensive for a nephrology provider to conduct alone. While this small pilot study demonstrated the role of pharmacist co-management in the setting of SGLT2 inhibitor use, a similar approach could be reasonably employed to help support the use of other therapies such as GLP-1 RAs and finerenone to improve CKD outcomes.

With the recent approval of finerenone, pharmacists can play an important role in educating patients and other members of the health care team concerning appropriate dosing, monitoring, and safety. As previously discussed, finerenone is approved to reduce the risk of sustained eGFR decline, ESRD, CV death, nonfatal myocardial infarction, and hospitalization for HF in adults with CKD associated with T2D. The manufacturer recommends that serum potassium and eGFR be monitored before initiation, and initiation is not recommended in patients with a serum potassium greater than 5.0 mEq/L. The recommended starting dose is 10 mg once daily in patients with an eGFR greater than or equal to 25 to less than 60 mL/min/1.73m², and 20 mg once daily in patients with an eGFR less than or equal to 60 mL/min/1.73m². Initiation is not recommended in patients with an eGFR less than 25 mL/min/1.73m². Monitoring of serum potassium is recommended 4 weeks after starting finerenone to guide dose adjustments.

Finerenone is a substrate of CYP3A4 and use is contraindicated in patients receiving concomitant treatment with strong CYP3A4 inhibitors, and it is recommended that concomitant intake of grapefruit or grapefruit juice be avoided. Use of finerenone with weak or moderate CYP3A4 inhibitors can also increase finerenone exposure and risk for increases in serum potassium, thus potassium monitoring is recommended with concomitant use upon drug initiation or dose adjustment of either finerenone or weak or moderate CYP3A4 inhibitors. The manufacturer also recommends avoiding concomitant use of strong or moderate CYP3A4 inducers, as concomitant use can result in reduced efficacy of finerenone.

With these considerations in mind, one specific pathway by which pharmacists can improve outcomes for patients with T2D and CKD is through medication therapy management (MTM) services. MTM involves assessing patients for medication-related problems, developing a patient-centered management plan, and providing appropriate follow-up. MTM services provided by a pharmacist may be useful in improving risk stratification and management of patients with T2D and CKD in the primary care setting. MTM services targeting current care gaps in patients with T2D and CKD, including underuse of recommended therapies (eg, ACE inhibitors and ARBs) and overuse of potentially nephrotoxic agents, provides an opportunity to improve care. Billing opportunities exist for MTM services through Medicare Part D plans, which include both diabetes and ESRD as core conditions, and for patients with stage 4 or 5 CKD through the new CMS Kidney Care Choices Model. With an expanding armamentarium of therapies to improve outcomes for patients with T2D and CKD, including novel nonsteroidal MRAs, pharmacists will undoubtedly play an important role in helping optimize medication use to improve the trajectory of DKD.

Conclusion
Optimal management of CKD in T2D incorporates a multifaceted approach to slow CKD progression and prevent kidney- and CV-related morbidity and mortality. New and emerging therapies, including SGLT2 inhibitors, GLP-1 RAs, and nonsteroidal MRAs, provide expanded therapeutic options to improve kidney and CV outcomes in
this high-risk population. Pharmacists can play an important role as members of the multidisciplinary management team to support utilization of these lifesaving therapies in individuals with T2D and CKD through patient-centered education, care coordination, and/or provision of clinical pharmacy services.

REFERENCES


22. American Diabetes Association. 5. Facilitating behavior change and well-being to improve

ADDITIONAL RESOURCES

American Diabetes Association Standards of Medical Care in Diabetes

Kidney Disease: Improving Global Outcomes (KDIGO) 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

American Society of Nephrology Diabetic Kidney Disease Collaborative

National Kidney Foundation Kidney Professionals page

National Kidney Foundation CKD Change Package

American Society of Nephrology Kidney Health Initiative

https://professional.diabetes.org/content-page/practice-guidelines-resources

https://kdigo.org/guidelines/diabetes-ckd/

www.asn-online.org/dkd-c/

www.kidney.org/professionals


https://khi.asn-online.org/


54. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular

114 PHARMACYTIMES.ORG AUGUST 2021


70. Study to Evaluate the Efficacy (Effect on Disease) and Safety of Finerenone on Morbidity (Events Indicating Disease Worsening) & Mortality (Death Rate) in Participants With Heart Failure and Left Ventricular Ejection Fraction (Proportion of Blood Expelled Per Heart Stroke) Greater or Equal to 40% (FINEARTS-HF). ClinicalTrials.gov. Updated June 23, 2021. Accessed July 16, 2021. clinicaltrials.gov/ct2/show/NCT04435626


NOTED: Your CE credit will be automatically uploaded to CPE Monitor. Please ensure that your Pharmacy Times® account is updated with your NABP e-profile ID number and your date of birth. Participation data will not be uploaded into CPE Monitor if you do not have your NABP e-profile ID number and date of birth entered into your profile on www.pharmacytimes.org.

SYSTEM REQUIREMENTS FOR COMPLETION:
Computer or smartphone with internet-access web browser (IE7.0+ or Webkit-/Mozilla-compatible) with JavaScript enabled.

FOR QUESTIONS ABOUT THIS INTERNET CPE ACTIVITY, PLEASE CONTACT: ceinfo@pharmacytimes.com.

PRIVACY POLICY AND TERMS OF USE INFORMATION: www.pharmacytimes.org/terms.
POSTTEST QUESTIONS

1. According to the CDC, which of the following are responsible for approximately 75% of new cases of kidney failure in the United States?
   A. Diabetes and hypertension
   B. Hypertension and retinopathy
   C. Diabetes and retinopathy
   D. Diabetes and dyslipidemia

2. Diabetic kidney disease (DKD) occurs in approximately _____ of patients with type 2 diabetes (T2D).
   A. 5%
   B. 25%
   C. 40%
   D. 90%

3. Renin-angiotensin system inhibitors improve outcomes in chronic kidney disease (CKD) through addressing which of the following pathophysiologic drivers of DKD?
   A. Hyperglycemia
   B. Glomerular hyperfiltration
   C. Mineralocorticoid receptor overactivation
   D. Production of advanced glycation end products

4. Overactivation of the mineralocorticoid receptor has been associated with promoting which of the following drivers of DKD progression?
   A. Hemodynamic dysregulation
   B. Inflammation and fibrosis
   C. Hyperglycemia
   D. Hypoglycemia

5. Kidney Disease: Improving Global Outcomes (KDIGO) recommends which of the following A1C targets for patients with T2D and CKD?
   A. <7.0% to <10.0%
   B. <7.0%
   C. <6.5%
   D. <6.5% to <8.0%

6. RJ is a patient with T2D currently managed with metformin monotherapy. His estimated glomerular filtration rate (eGFR) is 45 mL/min/1.73m² and his most recent labs indicate that he has severely increased albuminuria (urinary albumin-to-creatinine ratio [UACR] of 360 mg/gram creatinine). Per recommendations from KDIGO, an agent from which of the following glucose-lowering medication classes should be added to his regimen at this time to decrease his risk for CKD progression?
   A. Basal insulin (eg, insulin glargine)
   B. SGLT2 inhibitor
   C. Glucagon-like peptide-1 receptor agonist (GLP-1 RA)
   D. Dipeptidyl peptidase-4 (DPP-4) inhibitor

7. BG is a patient with T2D and CKD. His current A1C is 8.2%, but his provider would like to add a glucose-lowering therapy to his current regimen to see if he can achieve a lower A1C without hypoglycemia. BG is currently managed on metformin extended-release 500 mg twice daily plus dapagliflozin 10 mg once daily. His eGFR is 32 mL/min/1.73m². Which agent would be preferentially recommended at this time per current KDIGO recommendations?
   A. Long-acting GLP-1 RA
   B. DPP-4 inhibitor
   C. Pioglitazone
   D. Acarbose

8. Based on currently available clinical trial data, which of the following is true regarding finerenone?
   A. Finerenone caused significant increases in potassium compared with spironolactone, eplerenone, and placebo.
   B. Finerenone was less effective in lowering cardiac markers of hemodynamic stress but more effective at increasing eGFR in a majority of patients.
   C. Finerenone was associated with a higher incidence of worsening kidney function in participants aged 60 years and older but improved kidney function in younger adults.
   D. Finerenone significantly reduced risk of the composite primary kidney disease outcome (kidney failure, a sustained decrease in eGFR of ≥40% or death from kidney disease) in the FIDELIO-DKD trial.
POSTTEST QUESTIONS (continued)

9. In addition to CKD management, the National Kidney Foundation supports the development of multidisciplinary teams that incorporate pharmacists into the care path for management of which of the following?
   A. Potassium management
   B. Dialysis management
   C. Hypertension
   D. Case management

10. The CMS Kidney Care Choices Model provides billing opportunities for which of the following patient populations?
    A. Stage 1-2 CKD
    B. Stage 2-3 CKD
    C. Stage 3-4 CKD
    D. Stage 4-5 CKD
Product Hotline

CeraVe
Manufactured by L’Oreal
With products ranging from the Hydrating Facial Cleansers to the Itch Relief Moisturizing Lotion, CeraVe has options for all skin types and needs. Every product contains 3 essential ceramides to help restore the skin’s natural barriers, keeping moisture in and other elements out. Essential ingredients also include benzoyl peroxide, hyaluronic acid, niacinamide, retinol, and vitamin C. The products are also the No. 1 dermatologist-recommended according to the IQVIA ProVoice Survey and the No. 1 pharmacist-recommended product under the therapeutic skin care and moisturizers category in the 2021-2022 Pharmacy Times® OTC Guide Survey.

FOR MORE INFORMATION:
cerave.com

Shingrix
Manufactured by GlaxoSmithKline
With 99.5% of people ages 50 years and older infected with the varicella zoster virus, 1 in 3 people experience virus reactivation and shingles. Shingrix is indicated for the prevention of herpes zoster in older adults, and should be prioritized for this patient population, according to experts. Solicited local adverse reactions in subjects aged 50 years and older included pain (78%), redness (38.1%), and swelling (25.9%). General adverse reactions included myalgia (44.7%), fatigue (44.5%), headache (37.7%), shivering (26.8%), fever (20.5%), and gastrointestinal symptoms (17.3%).

FOR MORE INFORMATION:
shingrix.com

Reese’s Pinworm Medicine
Manufactured by Reese Pharmaceutical Company
As an over-the-counter option for pinworm treatments, Reese’s Pinworm Medicine offers a reliable treatment with up to 95% savings compared to a prescription medication. The formula contains pyrantel pamoate, which is the only over the counter anthelmintic recognized by the FDA. The treatment is available as a suspension and is indicated for patients ages 2 and older. It also has single dose effectiveness. Adverse effects can include abdominal cramps, nausea, vomiting, diarrhea, headache, or dizziness.

FOR MORE INFORMATION:
reesespinworm.com