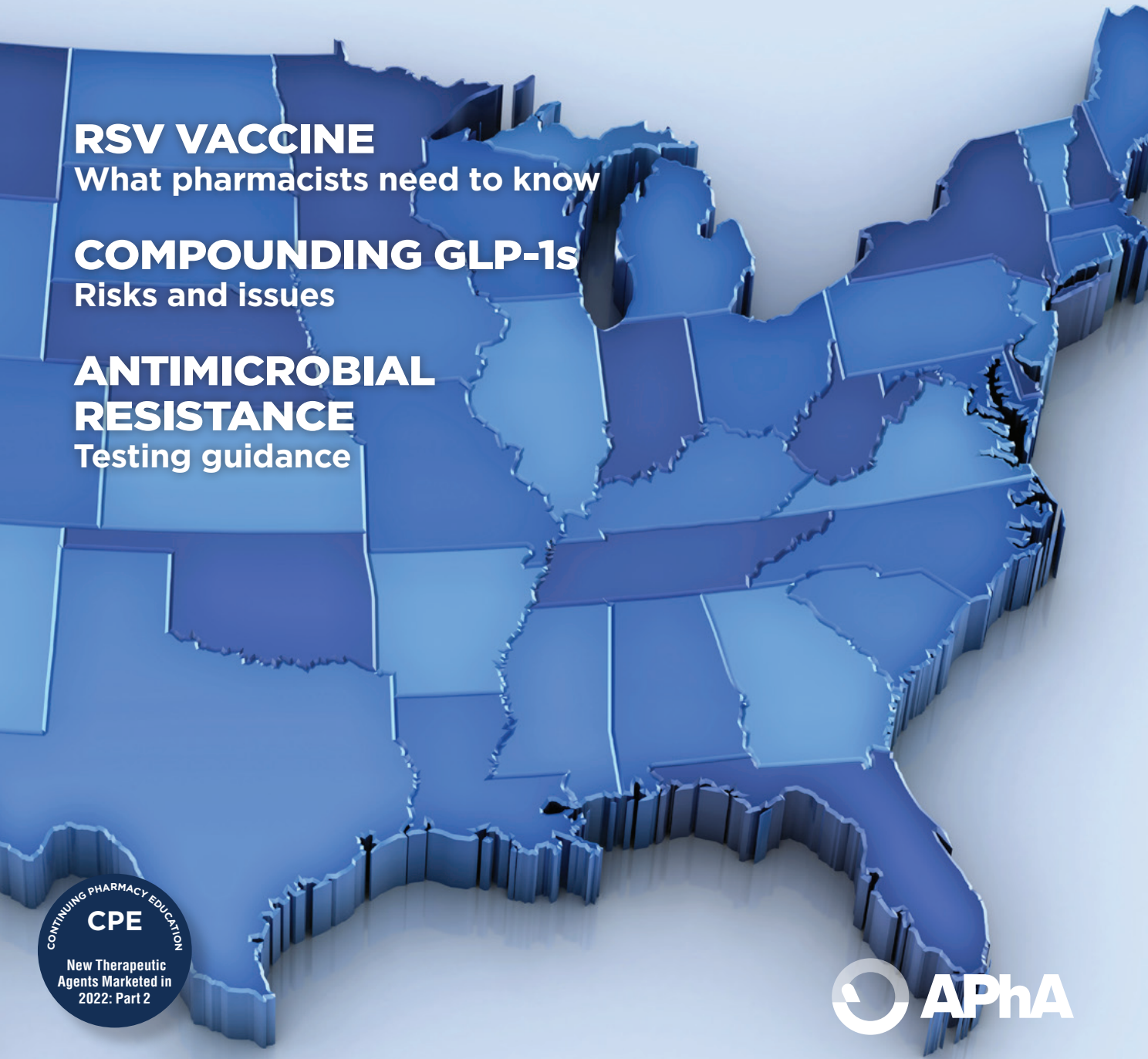
Pharmacy Today
An official publication of the American Pharmacists Association
AUGUST 2023

PROVIDER STATUS
EXPANDING PHARMACISTS' ROLES



RSV VACCINE
What pharmacists need to know

COMPOUNDING GLP-1s
Risks and issues

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Testing guidance

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CPE
New Therapeutic Agents Marketed in 2022: Part 2

APhA

BulletinToday

Researchers highlight 'vital role' of community pharmacists in public health

Community pharmacies in the United States "played a vital role in the public health response to the COVID-19 pandemic," said a new commentary published June 29, 2023, in *JAMA Forum*.

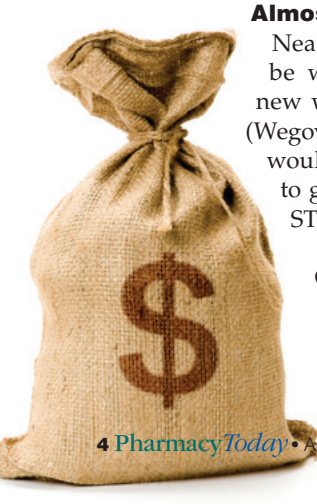
Citing data published earlier this year in *JAPhA*, authors of the new commentary wrote that from early 2021 to May 2023, community pharmacies provided more than 300 million doses of COVID-19 vaccines, representing more than two of every five doses administered in the United States.

"With this work, pharmacists delivered on a promise long recognized in the public health community, but seldom achieved in practice," wrote commentary authors Joshua Sharfstein, MD, from the Bloomberg School of Public Health at Johns Hopkins University, and Cherokee Layson-Wolf, PharmD, from the University of Maryland School of Pharmacy.

Their commentary lays out four clinical domains in which pharmacists are especially accessible and knowledgeable: HIV, hypertension, opioid overdose, and reproductive health care.

"The role of community pharmacists and pharmacies in the postpandemic world is uncertain. The special authority to provide COVID-19 testing and vaccination is scheduled to end in December 2024," Layson-Wolf and Sharfstein wrote. "As the clock ticks down, it is time to build for the future. There are more than 67,000 pharmacies in the U.S., with 88.9% of individuals living within 5 miles of at least one pharmacy. It is worth appreciating what this network could accomplish for the health, equity, and well-being of U.S. individuals, as reflected in the four clinical domains." ■

Almost one-half of Americans would spend $100 a month for weight loss drugs



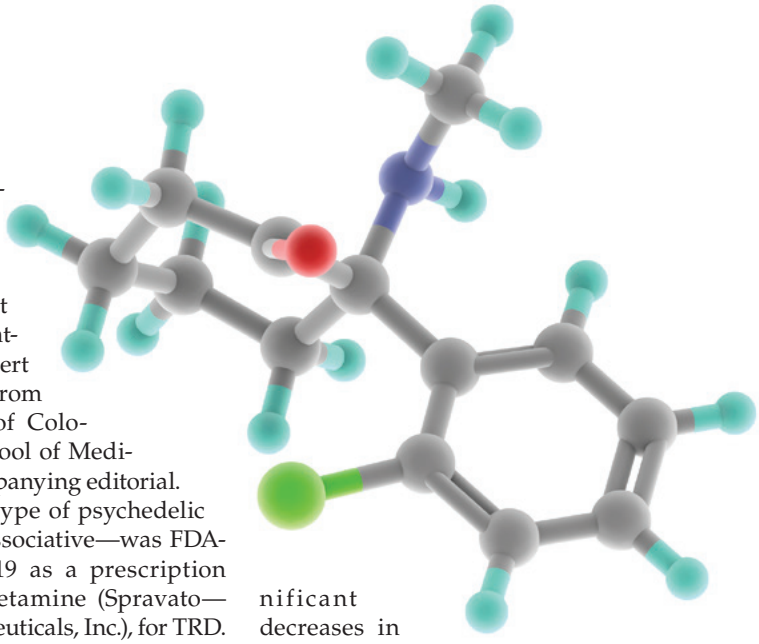
Nearly one-half of Americans said they would be willing to spend up to $100 a month for new weight loss medicines such as semaglutide (Wegovy—Novo Nordisk), and one-third said they would pay whatever they can afford indefinitely to get the drugs, according to a new survey by STAT and Harris Poll.

Demand is so great for the drugs, known as GLP-1 receptor agonists, that nearly one-quarter of respondents said they would pay up to $250 each month, with another 17% expressing a willingness to spend as much as $500 each month.

However, 84% believe insurance companies should cover the injectable medicines, which carry list prices ranging from $900 to $1,300 a month. Fewer than 25% of employers cover the medications, according to a 2022 survey of more than 500 employers.

The findings arrive as the medications have become a controversial sensation thanks to studies showing they can help people lose significant weight without causing notable adverse effects.

Nearly two-thirds of those surveyed indicated they would pursue one of the medicines to help improve their physical health, while 51% cited their self-image as a reason to do so. ■



Ketamine works just as well as 'gold standard' for treatment-resistant major depression, says study

A new study published June 22, 2023, in *NEJM* adds to the growing body of research on the effectiveness of ketamine for treatment-resistant depression (TRD). Results from the ELEKT-D randomized trial found that when it came to improving treatment-resistant major depression in outpatients without psychotic features, ketamine worked just as well as electroconvulsive therapy (ECT).

ECT and subanesthetic intravenous ketamine are both currently used for treatment-resistant major depression, but the comparative effectiveness of the two treatments remains uncertain.

The open-label trial randomized 403 patients with nonpsychotic treatment-resistant major depression to receive either ketamine or ETC.

"At the conclusion of the 3-week, randomized, active-treatment phase, 41% of the patients in the ECT group and 55% of those in the ketamine group reported a 50% or greater reduction in symptoms, findings that are consistent with moderate-to-excellent responses to treatment," wrote Robert Freedman, MD, from the University of Colorado Denver School of Medicine, in an accompanying editorial.

Ketamine—a type of psychedelic drug called a dissociative—was FDA-approved in 2019 as a prescription nasal spray, esketamine (Spravato—Janssen Pharmaceuticals, Inc.), for TRD. According to the official medication guidelines, it must be administered to patients under the supervision of a trained medical professional.

Study findings from 2019 published in the *American Journal of Psychiatry* first demonstrated the effectiveness of ketamine for TRD. Ketamine versus placebo resulted in clinically and statistically significant decreases in depression scores.

In both groups, patients continued taking antidepressants out of concern of not treating TRD. In another study from 2019 published in JAMA Psychiatry, researchers found that nasal ketamine had longer-term efficacy and helped patients stay in stable remission 16 weeks into treatment. ■

E-cigarette sales climb, according to new report

Sales of e-cigarettes increased by almost 50% from 2020 to 2022, according to a report published June 23, 2023, in CDC's *Morbidity and Mortality Weekly Report*. The report also found that after January 2020, sales of mint- and other-flavored prefilled cartridges died down, and disposable e-cigarettes in fruit, sweet, and other flavors increased. Disposable e-cigarettes in youth-appealing flavors are now more commonly sold than prefilled units.

Additionally, the total number of e-cigarette brands increased 46.2% during the study period, from 184 to 269.

"Increases in the number of available e-cigarette brands during the study period and changes observed in the top five brands during December 2022 reflect the dynamic nature of the e-cigarette market," wrote study authors in the report.

Among 184 brands, the top five in descending order of sales were JUUL, Vuse, NJOY, My Blu, and Puff for the 4-week period ending January 26, 2020. During the 4-week period ending December 25, 2022, the top five brands were Vuse, JUUL, Elf Bar, NJOY, and Breeze Smoke. Vuse, JUUL, NJOY, and My Blu are prefilled cartridge brands, while Puff, Elf Bar, and Breeze Smoke are disposable.

In the United States, the prevalence of e-cigarette use is markedly higher among youths and young adults than it is among adults. In 2021, 4.5% of all adults aged 18 years or older and 11.0% of young adults aged 18 to 24 years used e-cigarettes. During 2022, 14.1% of high school students used e-cigarettes.

Citing the appeal of flavored e-cigarettes to children, FDA announced in 2020 that it would prioritize enforcement against prefilled e-cigarettes in flavors other than tobacco and menthol based on the prevalence of use of these products among youth at the time. "The present study's findings indicate that after this announcement, retail sales of mint- and other-flavored prefilled cartridges halted while notable increases in sales of fruit- and mint-flavored disposable products occurred," the study authors noted. ■

CDC highlights drugs costs in new report

A June 2023 report from CDC indicates that millions of U.S. adults are not taking their medications as prescribed due to cost.

According to the data, more than 8% of U.S. adults ages 18 to 64 years, or roughly 9.2 million people, tried to save money by delaying a prescription refill, skipping doses, or taking less medication than prescribed.

Average drug costs did not increase in 2021, but the number of prescriptions did, which caused spending to rise. CDC also found that more than one-third of adults took at least three prescription medications in 2021, while data from IQVIA showed that overall prescription drug costs rose by nearly 5% from 2020 to 2021, to $63 billion.

The CDC report indicated that 23% of adults without health care coverage did not take their medications as prescribed to reduce costs, compared with <7% of people who had private insurance. People with disabilities were about three times more likely than those without disabilities to ration their medications, as were people with fair or poor health compared with those with good health.

Additionally, women were more likely to skip taking medications compared with men. For the study, researchers with the National Center for Health Statistics evaluated responses to the 2021 National Health Interview Survey, a representative survey of U.S. households. ■

Diabetes will be 'a defining disease of this century,' global cases set to exceed 1 billion by 2050

The prevalence of diabetes is expected to more than double by 2050, according to a new *Lancet* study published June 22, 2023. Approximately 1 in 10 people worldwide at that time will have diabetes, marking a 60% increase in the prevalence of the disease, said the study findings.

"Diabetes will be a defining disease of this century," wrote editors of the *Lancet* in an editorial. "How the health community deals with diabetes in the next two decades will shape population health and life expectancy for the next 80 years."

The increasing rates will be steered by T2D, which comprised 96% of cases of the disease globally in 2021.

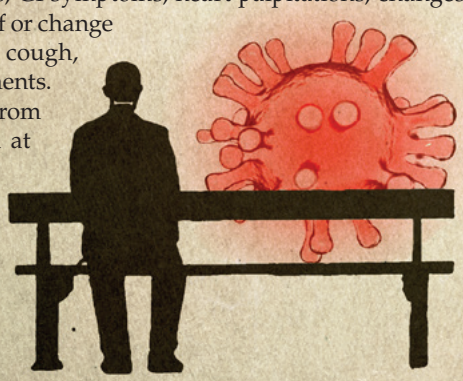
The *Lancet* study also suggested that T2D cases will be primarily associated with obesity. The authors attribute roughly one-half of the rise in diabetes over the next 3 decades to demographic shifts such as aging populations and to rising obesity rates. They also note that low- to middle-income countries are shifting to industrialized lifestyles that feature more processed foods and reduced physical activity. At the same time, people in these countries lack adequate access to treatments and are restricted in their health spending, the authors noted.

Referring to new drugs like semaglutide and tirzepatide, the authors said "the excitement and utility surrounding GLP-1 agonists and newer drug combinations that help to control blood sugar as well as reduce body weight is understandable. But…the solution to unhealthy and unfair societies is not more pills, but to re-evaluate and re-imagine our lives to provide opportunities to tackle racism and injustice and to prevent the major social drivers of disease." ■

Researchers better define long COVID

To better identify people with long COVID, researchers have identified 12 distinguishing symptoms and have developed a symptom-based scoring system.

Their report, published in the June 13, 2023, issue of *JAMA*, used survey data from nearly 10,000 individuals to define the symptoms: postexertional malaise, fatigue, brain fog, dizziness, GI symptoms, heart palpitations, changes in sexual desire or capacity, loss of or change in smell or taste, thirst, chronic cough, chest pain, and abnormal movements.



The researchers assessed data from a symptoms survey distributed at 85 hospitals, health centers, and community organizations across 33 states; Washington, DC; and Puerto Rico. The study included 8,646 people who contracted COVID-19 and 1,118 uninfected people who served as controls. ■

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CPE

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Daniel A. Hussar

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See solution at pharmacytoday.org

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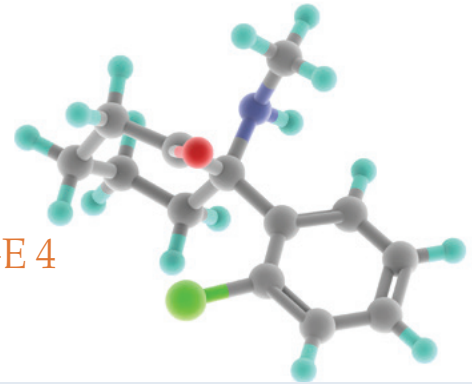

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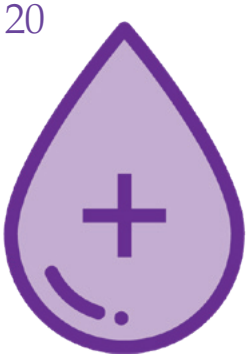

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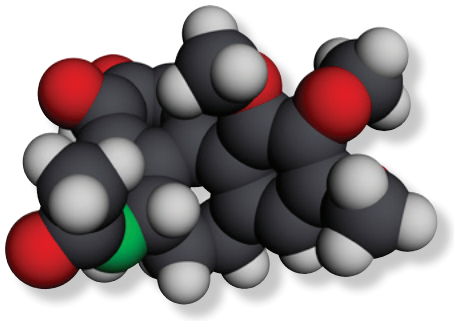


Provider status for pharmacists becoming a reality in many states

For the past 5 years, my clinical team and I have put extensive time and effort into obtaining payment for pharmacists' time for outpatient clinical pharmacogenomics visits. We conducted a successful pilot with the self-insured group within our health system, implemented a model in which pharmacists' time contributed to increased relative value unit-based physician compensation, utilized telehealth to reduce cost and overhead of the service, and initiated many other strategies. I would love to say these efforts have paved a path to compensation. Unfortunately, they have not. A little over a year ago, we transitioned to a patient self-pay model that has been successful. But in this and many other areas, pharmacists are limited in the patient care they can provide without having provider status.

Fortunately, this is changing. This month's *Pharmacy Today* cover story reviews the national landscape and progress in obtaining provider status and bringing pharmacists beyond the counter. From North Dakota's HB 1095 that allows for reimbursement of comprehensive medication management provided by pharmacists by health plans in the state to Virginia's SB 1538 that recognizes pharmacists as providers within the state Medicaid program and requires Medicaid to cover pharmacists' patient care services, things are looking up for pharmacists and their patients. Check out the cover story to see a full listing of state-by-state provider status changes.

In this issue, you'll also find the latest on newly approved drugs, including fezolinetant, a new nonhormonal therapy for hot flashes, and get an update on topical antibiotics and antiseptics. Find out what you need to know about the new respiratory syncytial virus vaccines, learn what's behind the surge in pediatric melatonin overdoses, and catch up on your CPE credit with this month's article on new therapeutic agents marketed in 2022.

In many ways, measures put in place to address immunization, testing, and treatment needs of the COVID-19 pandemic opened doors for expanding pharmacists' scope of practice. These strategies also changed patients' expectations about the value of care that their pharmacist could provide. It is welcome news that legal and regulatory steps are now being considered and passed in many states making many of these and other changes permanent for pharmacists and their patients. ■

Kristin Wiisanen
PharmD, FAPhA, FCCP
***Pharmacy Today* editor in chief**

APhA: Partnering to advance the profession

Often when I'm talking with student pharmacists or pharmacists at meetings or in the community, I hear "I sure wish our profession weren't so divided. Why can't we be unified like medicine?"

I think perhaps this perception comes from the fact that we have so many specialty organizations supporting pharmacists within a practice discipline. The reality is that in medicine there are well over 200 national professional organizations supporting physicians, far more than the fewer than 25 associations we have in pharmacy. Yet the question about how our national associations work together is an important one.

Founded in 1852 in Philadelphia, APhA is the oldest professional association in pharmacy; according to the American Society for Association Executives (yes, there is an association for associations!), APhA is one of the oldest associations of any type in the United States. As specialization bloomed within our profession, more specialty associations have formed, including the American Society of Health-System Pharmacists (ASHP), American Society of Consultant Pharmacists (ASCP), American College of Clinical Pharmacy (ACCP), Academy of Managed Care Pharmacy (AMCP), American Association of Psychiatric Pharmacists (AAPP), Pediatric Pharmacy Association (PPA), Hematology/Oncology Pharmacy Association (HOPA), National Community Pharmacists Association (NCPA), Society of Infectious Diseases Pharmacists (SIDP), American College of Apothecaries (ACA), American College of Veterinary Pharmacists (ACVP), and more.

All of these organizations are doing great work to move our profession forward through bringing pharmacists together, education, and advocacy. APhA is proud to call these associations and their leaders our friends and colleagues. Every day, APhA personnel actively collaborate with the staff and leaders of specialty organizations as well as other pharmacy organizations such as the American Association of Colleges of Pharmacy (AACP), the Accreditation Council for Pharmacy Education (ACPE), the National Association of Chain Drug Stores (NACDS), the National Association of State Pharmacy Associations (NASPA), the National Association of Boards of Pharmacy (NABP), the National Pharmaceutical Association (NPhA), Pharmacy Quality Alliance (PQA), and the United States Pharmacopeia (USP) to ensure our profession speaks with a unified voice. We actively collaborate with state pharmacy associations to directly support local efforts to advance the profession. Ultimately, we all want the same thing: to ensure patients have full access to the care services of pharmacists wherever they may practice.

A few ways in which we've collaborated just in the past several months include letters to DEA and FDA as well as urging DEA and the Substance Abuse and Mental Health Services Administration to clarify implementation of the Mainstreaming Addiction Treatment Act for prescribing pharmacists' training, among other ongoing joint advocacy efforts.

As the new CEO at APhA, I want pharmacists to know that our profession is more united than ever. We really do come together to speak with one voice with regulators and Congress. We collaborate on coalitions, task forces, and myriad initiatives too numerous to call out here. And even if you aren't a member, APhA represents you. We tirelessly provide a voice for every pharmacist, student pharmacist, and pharmacy team member—for all of pharmacy. We always have, and we always will. Won't you join us? ■

Michael D. Hogue
PharmD, FAPhA, FNAP, FFIP
Executive vice president and CEO of APhA

NEW DRUGS

RITLECITINIB
(Litfulo—Pfizer)

Drug class: Ritlecitinib is a kinase inhibitor.

Indication: Litfulo is indicated for the treatment of severe alopecia areata in adults and adolescents 12 years and older. It is not recommended for use in combination with other Janus kinase inhibitors (JAK inhibitors), biologic immunomodulators, cyclosporine, or other potent immunosuppressants.

Recommended dosage and administration: The recommended dosage is 50 mg orally once daily.

Common adverse effects: The most common adverse reactions are headache, diarrhea, acne, rash, urticaria, folliculitis, pyrexia, atopic dermatitis, dizziness, blood creatine phosphokinase increase, herpes zoster, red blood cell count decrease, and stomatitis.

Boxed warning: There is an increased risk of serious bacterial, fungal, viral, and opportunistic infections that may lead to hospitalization or death, including tuberculosis. Interrupt treatment if serious infection occurs until the infection is controlled. Litfulo should not be given to patients with active tuberculosis. Test for latent tuberculosis before and during therapy and start treating latent tuberculosis prior to use. Monitor all patients for active tuberculosis during treatment, even patients with initial negative latent tuberculosis test. Monitor all patients for signs and symptoms of infection during and after treatment with Litfulo. There is a higher rate of all-cause mortality, including sudden CV death with another JAK inhibitor versus tumor necrosis factor (TNF) blockers in patients with rheumatoid arthritis. Litfulo is not approved for use in patients with rheumatoid arthritis. Malignancies were reported in patients treated with Litfulo. There is a higher rate of lymphomas and lung cancers with another JAK inhibitor versus TNF blockers in patients with rheumatoid arthritis. There is a higher rate of major adverse CV events with another JAK inhibitor versus TNF blockers in patients with rheumatoid arthritis. Thrombosis has occurred in patients treated with Litfulo. There is an increased incidence of pulmonary embolism, and venous and arterial thrombosis with another JAK inhibitor versus TNF blockers.

Other warnings and precautions: Litfulo is contraindicated in patients with known hypersensitivity to ritlecitinib or any of its excipients. Discontinue Litfulo if a clinically significant hypersensitivity reaction occurs. Perform an absolute lymphocyte count (ALC) and platelet count prior to Litfulo initiation. Treatment interruption or discontinuation are recommended based on ALC and platelet count abnormalities. Avoid use of live vaccines during or shortly prior to Litfulo treatment. If taken concomitantly with certain CYP3A substrates or certain CYP1A2 substrates, additional monitoring and dose adjustments of the substrate should be considered. Coadministration with strong inducers of CYP3A is not recommended. Breastfeeding is not recommended. The use of Litfulo in severe hepatic impairment is not recommended.

NEW INDICATIONS

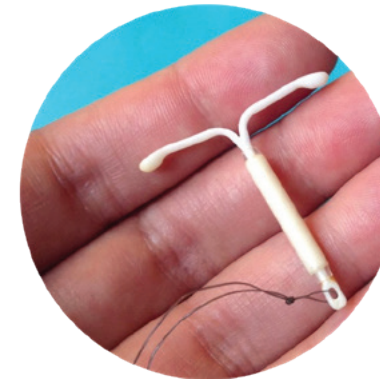
LEVONORGESTREL-RELEASING INTRAUTERINE SYSTEM
(Liletta—Medicines360)

Drug class: Liletta is a progestin-containing intrauterine system.

Indication: Liletta is indicated for prevention of pregnancy for up to 8 years and treatment of heavy menstrual bleeding for up to 5 years in patients who choose intrauterine contraception as their method of contraception.

Recommended dosage and administration: The initial release rate of levonorgestrel is approximately 20 µg/day and declines progressively to approximately 6.5 µg/day after 8 years. Liletta can be removed at any time but must be removed by the end of the eighth year. Liletta should be inserted into the uterine cavity with the provided inserter by a trained health care professional using aseptic technique. Follow insertion instructions exactly as described. Re-examination and evaluation should be considered 4 to 6 weeks after insertion and during routine care, or more often if clinically indicated.

Common adverse effects: The most common adverse reactions reported in clinical studies were vulvovaginal mycotic infections, vaginal bacterial infections, acne, and nausea or vomiting.



Warnings and precautions: Liletta is contraindicated in pregnancy, congenital or acquired uterine anomaly that distorts the uterine cavity and would be incompatible with correct intrauterine system placement; acute pelvic inflammatory disease; postpartum endometritis or infected abortion in the past 3 months; known or suspected uterine or cervical malignancy; known or suspected breast cancer or other hormone-sensitive cancer; uterine bleeding of unknown etiology; untreated acute cervicitis, vaginitis, or other lower genital tract infections; acute liver disease or liver tumor; increased susceptibility to pelvic infections; a previously inserted intrauterine system that has not been removed; and hypersensitivity to any component of Liletta. Additionally, Liletta should not be used for postcoital or emergency contraception. Remove Liletta if pregnancy occurs with Liletta in place and Liletta is in the uterus. If pregnancy occurs, there is increased risk of ectopic pregnancy, pregnancy loss, septic abortion, and premature labor and delivery. Severe infection or sepsis, including Group A streptococcal sepsis, have been reported following insertion of levonorgestrel-releasing intrauterine systems. Strict

aseptic technique is essential during insertion. Before using Liletta, consider the risks of pelvic infection. Perforation may occur and reduce contraceptive effectiveness or require surgery. Risk is increased if inserted in patients who have fixed retroverted uteri, are postpartum, or are lactating. Partial or complete expulsion may occur. Evaluate persistent enlarged ovarian follicles or ovarian cysts. Bleeding patterns can become altered, may remain irregular, and amenorrhea may ensue.

ODEVIXIBAT

(Bylvay—Albireo)

Drug class: Bylvay is an ileal bile acid transporter.

Indication: Bylvay is indicated for the treatment of pruritus in patients 3 months and older with progressive familial intrahepatic cholestasis (PFIC) and the treatment of cholestatic pruritus in patients 12 months and older with Alagile syndrome (ALGS).

Recommended dosage and administration: For use in PFIC, the recommended dosage is 40 µg/kg taken orally once daily in patients 3 months and older. If there is no improvement in pruritus after 3 months, the dosage may be increased in 40 µg/kg increments up to 120 µg/kg once daily, not to exceed a daily dosage of 6 mg/day. For use in ALGS, the recommended dosage is 120 µg/kg taken orally once daily. Administer Bylvay in the morning with a meal. Do not crush or chew the capsules.

Common adverse effects: The most common adverse reactions are liver test abnormalities, diarrhea, abdominal pain, vomiting, fat-soluble vitamin deficiency, hematoma, and decreased weight.

Warnings and precautions: Based on animal data, use of Bylvay during pregnancy may cause cardiac malformations. Obtain baseline liver tests and monitor patients during treatment. Dose reduction or treatment interruption may be required if abnormalities occur. For persistent or recurrent liver test abnormalities, consider treatment discontinuation. Treat dehydration. Treatment interruption or discontinuation may be required for persistent diarrhea. Obtain baseline levels of fat-soluble vitamins and monitor during treatment. Supplement if deficiency is observed. If deficiency persists or worsens despite supplementation, discontinue treatment.

NEW COMBINATIONS

POLYETHYLENE GLYCOL 3350, SODIUM SULFATE, POTASSIUM CHLORIDE, MAGNESIUM SULFATE, AND SODIUM CHLORIDE FOR ORAL SOLUTION

(Suflave—Braintree Labs)

Drug class: Suflave is an osmotic laxative.

Indication: Suflave is indicated for cleansing of the colon in preparation for colonoscopy in adults.

Recommended dosage and administration: Administration of two doses of Suflave is required for a complete preparation for colonoscopy. One dose of Suflave is equal to one bottle plus one flavor-enhancing packet. Each bottle must be reconstituted with water before ingestion. An additional 16 oz of water must be consumed after each dose. Stop consumption of all fluids at least 2 hours before the colonoscopy. The recommended split-dose regimen consists of two doses over 2 days. The evening before colonoscopy, one bottle with the flavor-enhancing packet should be ingested. On the morning of the colonoscopy, 5–8 hours prior to the colonoscopy and no sooner than 4 hours from the first dose, one bottle with the flavor-enhancing packet should be ingested.

Common adverse effects: The most common adverse reactions are nausea, abdominal distension, vomiting, abdominal pain, and headache.

Warnings and precautions: Suflave is contraindicated in patients with a GI obstruction or ileus, bowel perforation, toxic colitis or toxic megacolon, gastric retention, or hypersensitivity to any ingredient in Suflave. Adequate hydration should be encouraged, concurrent medications should be assessed, and laboratory assessments should be considered prior to and after each use and there is risk of fluid and electrolyte abnormalities. Consider predose and postcolonoscopy ECGs in patients at increased risk of cardiac arrhythmias. Use caution in patients with a history of seizures and patients at increased risk of seizures, including medications that lower the seizure threshold. Consider potential for ulcerations when interpreting colonoscopy findings in patients with known or suspected inflammatory bowel disease. Use caution, ensure adequate hydration, and consider laboratory testing in patients with renal impairment or taking concomitant medications that affect renal function. If a GI obstruction or perforation is suspected, rule out the diagnosis before administration. Observe patients at risk for aspiration during administration. Inform patients to seek immediate medical care if symptoms of hypersensitivity reactions, including anaphylaxis, occur. ■

Also in this issue
FDA approves new buprenorphine treatment option for OUD (page 23)

Topical antibiotics and antiseptics

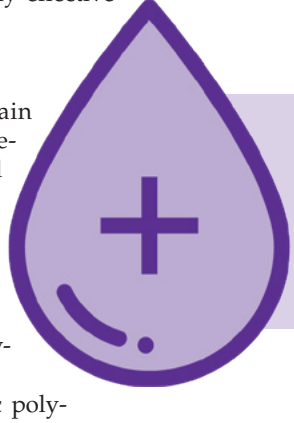
Mary Warner

A tube of nonprescription antibiotic ointment or bottle of antiseptic is a staple in most medicine cabinets, and for good reason. These products can prevent infection of small cuts, scrapes, or other skin injuries that don't require medical intervention.

Although nonprescription antibiotics and antiseptics are often thought of as being similar, there are important differences between them. Antiseptics inhibit the growth of bacteria on the skin's surface, while antibiotics kill bacteria directly. And while antiseptics can target bacteria, viral species, and fungi, antibiotics are only effective against bacteria.

Active ingredients

Nonprescription antibiotics contain one or more of three active ingredients—bacitracin, neomycin, and polymyxin B sulfate—with triple antibiotic ointment being the most commonly available. Each of these medications targets specific bacteria, which gives the triple antibiotic ointment a wide spectrum of activity.



Bacitracin is a mixture of cyclic polypeptides produced by *Bacillus licheniformis*. It targets gram-positive bacteria, especially those that cause skin infections such as *Staphylococcus aureus*, *Staphylococcus epidermis*, and *Streptococcus pyogenes*. It disrupts cell-wall synthesis by interfering with the lipids that transport the building blocks of the peptidoglycan cell wall.

Neomycin is an aminoglycoside antibiotic that inhibits bacterial protein synthesis of gram-negative bacteria, while polymyxin B sulfate alters bacterial outer membrane permeability resulting in leakage of cellular molecules and inhibition of cellular respiration in gram-negative bacteria.

Antiseptics contain either benzalkonium, iodine admixtures, alcohol, or hydrogen peroxide, all of which affect the cellular envelope of the microorganism or interfere with critical enzyme processes.

How effective are they?

Results of published research on the efficacy of nonprescription topical antibiotics and antiseptics are mixed. A 2011 study published in the *Journal of the American Academy of Dermatology* compared the wound-healing properties of a topical emollient with that of an antibiotic ointment containing neomycin, bacitracin and polymyxin and an antibiotic ointment containing bacitracin and polymyxin B and found that the nonantibiotic emollient cream was equally as effective as the topical antibiotics in healing wounds and preventing infection.

> Antiseptics inhibit the growth of bacteria on the skin's surface, while antibiotics kill bacteria directly.

A 2018 systematic review published in *Infection and Drug Resistance* analyzed 10 studies comparing topical antibiotics with placebo and four studies that compared antiseptics with antibiotics. The authors found that topical antibiotics were effective in reducing the risk of infections in uncomplicated wounds compared to placebo or antiseptics, but the absolute risk reduction was minimal compared to that with

Trade name	Formulation	Active ingredient(s)
Neosporin and generics	Antibiotic ointment	Bacitracin zinc, neomycin sulfate, polymxyin B sulfate
Simply Neosporin	Antibiotic ointment	Bacitracin zinc, polymxyin B sulfate
Neosporin Pain	Antibiotic ointment, cream	Bacitracin zinc, polymxyin B sulfate, pramoxine HCL
Polysporin	Antibiotic ointment	Bacitracin zinc, polymxyin B sulfate
Bacitracin	Antibiotic ointment	Bacitracin zinc
Neosporin spray	Antiseptic spray	Benzalkonium Cl 0.13%, pramoxine HCL 1%
Band-Aid antiseptic spray	Antiseptic spray	Benzalkonium Cl 0.13%, pramoxine HCL 1%
Bactine	Antiseptic liquid	Benzalkonium Cl 0.13%
Merthiolate	Antiseptic liquid	Benzalkonium Cl 0.13%
Povidone-Iodine sticks	Antiseptic swab stick	Povidone-iodine 10%
Povidone-Iodine	Antiseptic liquid	Povidone-iodine 10%
Iodine tincture	Antiseptic liquid or spray	Iodine 2%, sodium iodide 2.4%, alcohol 47%
Hydrogen peroxide	Antiseptic liquid or spray	Hydrogen peroxide 3%
Alcohol	Antiseptic liquid	Isopropyl alcohol 91%

a placebo. In addition, there was no statistically significant absolute reduction when compared to antiseptics.

Availability

Topical antibiotics are available as creams or ointments, while antiseptics are available as liquids and sprays. Ointments are appropriate for minor burns and wounds in which the skin is intact because they maintain a moist healing environment. Creams are most appropriate for cuts and scrapes as they allow some fluid to pass through the film.

To prevent contaminating the medication, the patient should not apply ointments and creams directly from the container onto the burn or wound, but rather apply the product to a clean hand or gauze and then apply it to the site of the injury. Liquid antiseptics should be applied using gauze or a cotton ball, while antiseptic sprays should be held approximately 6 inches from the skin while spraying for 1 to 3 seconds.

What to tell your patients

Ensure that patients understand the difference between a topical antibiotic and an antiseptic to confirm that they are using the appropriate product for their situation. Although topical antibiotics and antiseptics are well tolerated and carry a minimal risk of hypersensitivity, advise patients to contact their health care provider if they experience contact dermatitis.

Finally, because of the increasing importance of antimicrobial stewardship, judicious use of topical antibiotics is prudent, and antiseptics should be considered as a reasonable alternative to topical antibiotics.

For further information, see Chapter 41 in *APhA's Handbook of Nonprescription Drugs*, available in the bookstore on pharmacist.com or in PharmacyLibrary. ■

Black pepper extract and CYP3A4 inhibition

Mickie Cathers

Piperine, a major component of black pepper (*Piper nigrum*), is responsible for black pepper's distinct flavor, is what makes you sneeze, and gives black pepper its reputation for having antioxidant and anti-inflammatory properties. Piperine supplements are advertised as enhancing nutrient absorption and relieving inflammation (especially when taken with turmeric). Patients taking this supplement may not be aware that piperine interacts with certain drugs.

Background

Black pepper is a climbing perennial plant known worldwide as both a spice and a medicine. Black pepper contains ~2–7% piperine, which gives it pharmacologic effects and health benefits ranging from cancer and diabetes prevention; improved digestion; weight loss; BP control; relief from coughs, colds, and infections; and enhanced brain, hair, and skin health. Black pepper extract is promoted as an antioxidant that maximizes nutrient absorption—especially vitamin C by up to 50% and turmeric as much as 2,000%—and aids in heart health, digestive health, and optimized gut flora.

Many studies have shown that piperine results in antioxidant, antidiabetic, antimicrobial, anti-inflammatory, and gastro- and cardioprotective activities. The alkaloid functionality of piperine assists in cognitive brain functioning and helps stimulate hydrochloric acid in the stomach, which aids in digestion and food absorption, reducing discomfort and gas buildup in the intestines. Studies have also shown that piperine has free-radical scavenging activities and antitumor properties.

Piperine's dark side

Despite the reported benefits of piperine in the literature, there is evidence of adverse influence on the liver. Piperine may change how quickly the liver breaks down medications such as cytochrome P450 sA4 (CYP3A4) substrates. Piperine may also affect how P-glycoprotein substrates transport medication in and out of cells.

Preliminary data have indicated that piperine inhibited drug-metabolizing enzymes and increased plasma concentrations of several drugs, including phenytoin and rifampin. A 2002 research article published in the *Journal of Pharmacology and Experimental Therapeutics* investigated the influence of piperine on P-glycoprotein–mediated, polarized transport of digoxin and cyclosporine in monolayers of Caco-2 cells.

Bhardwaj and colleagues showed that piperine inhibited both the drug transporter P-glycoprotein and the major drug-metabolizing enzyme CYP3A4, indicating that dietary piperine could affect plasma concentrations of P-glycoprotein and CYP3A4 substrates, especially if these drugs are administered orally.

A review in *Critical Reviews in Food Science and Nutrition* in 2007 by Srinivasan backed up the findings of Bhardwaj and colleagues' article, highlighting piperine's inhibitory influence on enzymatic drug reactions in the liver.

Piperine may change how quickly the liver breaks down medications such as cytochrome P450 sA4 (CYP3A4) substrates.

Dosages and availability

There is no recommended appropriate dose of piperine. Piperine supplements are sold as capsules, gummies, liquid, pills, powder, and tablets and are often marketed in combination with turmeric, ashwagandha, or CoQ10. Most piperine supplements are available commercially as 10 mg capsules to be taken three times per day for a total of 30 mg per day.

What to tell patients

Black pepper sprinkled on food can be enjoyed without concern. However, caution patients that piperine supplements are concentrated forms of black pepper and could change how quickly the liver breaks down medications and increase the chances of adverse effects from some medications. Common adverse effects of piperine include acid reflux, constipation, low potassium levels, and nausea. Contraindications include use with lithium, as piperine may decrease how well the body releases lithium. Piperine may lower blood glucose levels and could cause complications for patients taking diabetes medications. Piperine could also increase levels of atorvastatin in the blood and increase both its therapeutic and adverse effects. ■

New buprenorphine treatment option

Lauren Howell, PharmD

In May of 2023, FDA approved Brixadi (Braeburn Inc.), a new dosage form of the partial opioid agonist buprenorphine. This extended-release injection for subcutaneous use is indicated for the treatment of moderate to severe opioid use disorder (OUD) in patients who have initiated treatment with a single dose of a transmucosal buprenorphine product or who are already being treated with buprenorphine. This approval expands treatment options for patients looking to sustain long-term recovery from OUD.

Recommended dosage and administration

Brixadi should only be prepared and administered by health care providers. Doses should be administered slowly into the subcutaneous tissue of the buttock, thigh, abdomen, or upper arm. Providers should consider prescribing naloxone when Brixadi is initiated or renewed, since patients being treated for OUD have the potential for relapse, putting them at risk for opioid overdose.

Brixadi is available in both a weekly and monthly formulation. In patients who are not already receiving buprenorphine treatment, the recommended weekly dose is 24 mg titrated up over the first week of treatment.

A test dose of transmucosal buprenorphine 4 mg should be administered when objective signs of mild to moderate withdrawal appear. If the dose of transmucosal buprenorphine is tolerated without precipitated withdrawal, the first 16 mg dose of Brixadi (weekly) can be administered. An additional 8 mg dose of Brixadi (weekly) should be administered within 3 days of the first dose to achieve the recommended 24 mg Brixadi (weekly) dose.

If needed, an additional 8 mg dose can be administered during this first week as long as it is at least 24 hours after the previous injection. Subsequent Brixadi (weekly) injections can be administered based on the total weekly dose that was established during the first week of treatment. Adjustments can be made at weekly appointments with the maximum weekly dose being 32 mg. Patients who are already being treated with a buprenorphine-containing product may be switched directly to either the weekly or monthly Brixadi formulation.

Patients may also be transitioned from weekly to monthly or from monthly to weekly dosing based on clinical judgment. However, since Brixadi (weekly) and Brixadi (monthly) are different formulations, doses of the weekly formulation cannot be combined to yield an equivalent monthly dose.

For details on the recommended Brixadi weekly or monthly doses based on the corresponding daily doses of sublingual buprenorphine, please see the chart below.

Daily doses of sublingual buprenorphine and suggested Bridaxi doses

Daily dose of sublingual bupenorphine	Brixadi weekly dose	Brixadi monthly dose
≤6 mg	8 mg	—
8–10 mg	16 mg	64 mg
12–16 mg	24 mg	96 mg
18–24 mg	32 mg	128 mg

Adverse effects

The most common adverse reactions associated with Brixadi administration were injection site pain, headache, constipation, nausea, injection site erythema, injection site pruritus, insomnia, and UTI. Patients should be monitored for conditions indicative of diversion or progression of opioid dependence and addictive behaviors.

Life-threatening respiratory depression and death have occurred in association with buprenorphine. Patients should be warned of the potential danger of self-administration of benzodiazepines and other central nervous system depressants while under treatment with Brixadi.

Neonatal opioid withdrawal syndrome is an expected and treatable outcome of prolonged use of opioids during pregnancy. If adrenal insufficiency is diagnosed, treat with physiologic replacement of corticosteroids, and wean the patient off the opioid. If treatment with Brixadi is discontinued, monitor patients for withdrawal and treat appropriately. Monitor liver function tests prior to and during treatment. The packaging of this product contains natural rubber latex which may cause allergic reactions. Treat pain with a non-opioid analgesic whenever possible. If opioid therapy is required, monitor patients closely because higher doses may be required for analgesic effect.

Clinical trials

The safety and efficacy of Brixadi were evaluated in a randomized, double-blind, active-controlled clinical trial. A total of 428 patients with a diagnosis of moderate to severe OUD received an initial test dose of transmucosal buprenorphine and were then randomized to treatment with Brixadi plus a sublingual placebo, or active sublingual buprenorphine plus placebo injections. Patients were treated with weekly injections over 12 weeks and then transitioned to monthly injections for an additional 12 weeks. Urine drug screening and self-reporting of illicit opioid use during treatment were used to measure response to treatment. If patients completed each of the two phases with negative opioid assessments, they were considered a responder. In the Brixadi group, 16.9% of patients met the responder definition compared to 14.0% in the sublingual buprenorphine group. ■

FDA approves RSV vaccine

Lauren Howell, PharmD

Since May 2023, FDA has approved two respiratory syncytial virus (RSV) vaccines; the first time a vaccine for RSV has been approved for use in the United States. According to CDC, RSV leads to approximately 60,000 to 120,000 hospitalizations and 6,000 to 10,000 deaths among adults 65 years and older each year in the United States.

Both Arexvy (GSK) and Abrysvo (Pfizer) were approved for the prevention of lower respiratory tract disease caused by RSV in individuals 60 years and older. They are both injected intramuscularly as a single 0.5 mL dose. The most commonly reported adverse reactions for both vaccines.were injection site pain, fatigue, myalgia, headache, and arthralgia

Clinical trials for Arexvy

The efficacy of Arexvy against RSV-associated lower respiratory tract disease in adults 60 years and older was evaluated in an ongoing, Phase 3, randomized, placebo-controlled, observer-blind clinical study conducted in 17 countries. While immunocompromised participants were excluded from the study, participants with pre-existing, chronic, stable disease were allowed to participate in the study if deemed medically stable at the time of vaccination. The 24,960 participants were randomized equally to either receive one dose of Arexvy or placebo. Study authors plan to follow participants for up to 36 months but at the time of primary efficacy analysis, they had been followed for up to 10 months.

Compared with placebo, Arexvy significantly reduced the risk of developing RSV-associated lower respiratory tract disease by 82.6% in participants 60 years and older. In participants 70 years and older, the risk was reduced by 84.4%. Additionally, Arexvy reduced the risk of developing severe RSV-associated lower respiratory tract infections by 94.1%. The median duration of efficacy follow-up was 6.7 months.

Clinical trials for Abrysvo

The efficacy of Abrysvo in individuals 60 years and older was evaluated in an ongoing, Phase 3, multicenter, randomized, double-blind, placebo-controlled study. Study authors plan to follow patients for up to two RSV seasons, approximately 25 months. Randomization was stratified by age: 60 to 69 years, 70 to 79 years, and those 80 years and older. Healthy adults and adults with stable chronic diseases were included. Out of the enrolled participants, 15% had stable chronic cardiopulmonary conditions. Beginning 14 days after vaccination, participants were monitored for onset of acute respiratory illness symptoms. The median duration of follow-up for efficacy was 7 months.

Compared with placebo, Arexvy significantly reduced the risk of developing RSV-associated lower respiratory tract disease by 82.6% in participants 60 years and older.

The study split episodes of RSV-associated lower respiratory tract disease into two groups, those with two or more symptoms and those with three or more symptoms. Researchers observed 11 cases of RSV-associated lower respiratory tract disease with two or more symptoms in patients given Abrysvo and 33 in patients given a placebo, a vaccine efficacy of 66.7%. Only 2 cases of RSV-associated lower respiratory tract disease with three or more symptoms occurred in patients given Abrysvo and 14 cases in patients given a placebo, resulting in a vaccine efficacy of 85.7%.

Role of the pharmacist

With the new vaccines expected to be available this fall, pharmacists can play a large role in helping patients to understand the potential benefits and risks of vaccination with Abrysvo or Arexvy.

Pharmacists should inform patients over the age of 60 years about the dangers of RSV-associated lower respiratory tract disease. They can also remind patients of the dangers of spreading RSV to other loved ones, particularly babies who are especially vulnerable to RSV.

Additionally, while these trials are ongoing and information is still being collected, it is important that pharmacists remember to encourage patients to report any adverse events to their health care provider or to the Vaccine Adverse Event Reporting System. ■

First-in-class fezolinetant brings women a new nonhormonal therapy for hot flashes

Sonya Collins

FDA approved fezolinetant (Veozah–Astellas Pharma US), a first-in-class neurokinin 3 (NK3) receptor antagonist, for the treatment of moderate to severe vasomotor symptoms (VMS) of menopause in May 2023. Marking an expansion in women's nonhormonal options for the treatment of these symptoms, fezolinetant is now the second FDA-approved nonhormonal treatment for hot flashes and night sweats, after the SSRI paroxetine (Brisdelle–Noven Pharmaceuticals).

"Despite hormone therapy being the most efficacious treatment of vasomotor symptoms, such as hot flashes, some may be unable or unwilling to use it due to contraindications or perception of risks," said Nicole Cieri-Hutcherson, PharmD, BCPS, NCMP, a clinical assistant professor at the University at Buffalo School of Pharmacy and Pharmaceutical Sciences, who has a special focus on women's health. "Unfortunately, efficacious, nonhormonal options are lacking."

Fezolinetant offers women an additional nonhormonal option.

New drug class

Fezolinetant is an NK3 receptor antagonist. The NK3 pathway regulates the secretion of gonadotropin releasing hormone (GnRH) and plays a role in the brain's regulation of body temperature and, as a result, the generation of hot flashes. Fezolinetant binds to and blocks the activities of NK3 receptors to prevent hot flashes.

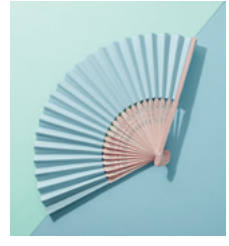
In Phase 3 clinical trials, the most common adverse effect of this drug was headache.

"With earlier medications in the same class, significant elevations in hepatic enzymes were seen," Cieri-Hutcherson said. "However, with fezolinetant, elevations in hepatic enzymes were rare and resolved either during treatment continuation or treatment discontinuation."

New, nonhormonal option

Up to 80% of women experience hot flashes during menopause, which can last for several years and have a significant impact on quality of life.

While hormone therapy is the gold standard for treatment of VMS, those who have a history of vaginal bleeding, stroke, heart attack, blood clots, or liver disease are not candidates for this medication. Other women may be unwilling to take hormone therapy based on the risks associated with it, which some perceive to be high. Paroxetine, which also comes with risks of adverse effects and interactions as well as contraindications that patients and providers must consider, has been the only FDA-approved nonhormonal option for patients in this population until now.



"Fezolinetant represents an expansion to the efficacious pharmacotherapeutic armamentarium for the management of vasomotor symptoms."

"Fezolinetant represents an expansion to the efficacious pharmacotherapeutic armamentarium for the management of vasomotor symptoms," said Cieri-Hutcherson.

It should be noted, however, that while hormone therapy addresses several symptoms of menopause, fezolinetant is only proven effective for treating hot flashes and night sweats.

"Fezolinetant's impact on mood, genitourinary, sexual, cardiovascular, metabolic, and bone health remain to be seen," Cieri-Hutcherson said. "Further studies are needed in larger populations to elucidate this."

Expanding the nonhormonal armamentarium

Fezolinetant joins a small but potentially growing number of evidence-based pharmaceutical and nonpharmaceutical therapies for menopause symptoms.

The North American Menopause Society (NAMS) recently released a position statement on these options developed by an advisory panel of researchers with expertise in nonhormone medical therapy, herbal therapy, behavioral therapy, and lifestyle approaches for VMS. The recommendations were based on their evaluation of all available literature on these therapies since the publication of NAMS' last position statement in 2015.

In addition to fezolinetant, the panel recommended cognitive behavioral therapy, clinical hypnosis, weight loss, stellate ganglion blockade, SSRIs/serotonin-norepinephrine reuptake inhibitors, gabapentin, and oxybutynin.

Among those approaches for which the panel did not find sufficient evidence were paced respiration, supplements and herbal remedies, cooling techniques, avoiding triggers, exercise, yoga, mindfulness-based intervention, relaxation, suvorexant, soy products, cannabinoids, acupuncture, calibration of neural oscillations, chiropractic interventions, clonidine, dietary modification, and pregabalin.

"The good news for women is that there are many options available for the treatment of bothersome hot flashes, including several nonhormone therapies," Stephanie Faubion, MD, NAMS medical director, said in a press release. "We also have a better understanding of what is not effective so that women and health care professionals can target therapies that have been proven to work and avoid the wasted time, energy, and expense associated with ineffective or unproven remedies." ■

What pharmacists need to know as pediatric melatonin overdoses surge

Sonya Collins

The number of annual calls to poison control for pediatric melatonin overdoses increased by a whopping 530% from 2012 to 2021. These were the findings of a cross-sectional study of pediatric melatonin ingestions reported to U.S. poison control centers published in CDC's *Mortality and Morbidity Weekly Report* (*MMWR*) in June 2022.

Researchers and health care providers tend to attribute the surge in part to both the uptick in sleep troubles children experienced during the COVID-19 pandemic, and the supplement often coming in a gummy form that's easily mistaken for candy.

Not all the symptoms of pediatric melatonin overdose are benign. Two deaths associated with the supplements were reported in the *MMWR* data. Pharmacists should take every opportunity to educate parents on the safe use of melatonin in children.

OTC supplements aren't always what they say they are

While most reports of melatonin overdoses in children involve mild symptoms, such as drowsiness, nausea, and vomiting, 287 children recorded in the *MMWR* study were admitted to ICUs for ingestions; five required ventilators; and two died.

As melatonin in high doses is not known to cause such serious effects, these outcomes serve as a reminder that the ingredients in OTC supplements are not always exactly as they are listed on their labels.

According to Cydney McQueen, PharmD, clinical associate professor at University of Missouri-Kansas City School of Pharmacy, pharmacists should advise patients, parents, and caregivers that when buying supplements for children, they should buy only brands that carry the seal indicating that the manufacturer participates in USP's Dietary Supplement Verification Program.

"That is an indicator that the manufacturing facilities are being inspected and the products are regularly tested to make sure they contain what the label states," said McQueen, who has expertise in natural medicines and dietary supplements.

Recent research confirms that the labels on melatonin products cannot always be trusted. A *JAMA* study from April 2023 that analyzed 25 brands of gummies found significant variation in contents across products, and major discrepancies between the amount of active ingredient listed on the label and that contained in the gummy.

One product contained no detectable melatonin but rather 31.3 mg of CBD. The quantity of melatonin in the other gummies ranged from 74% to 347% of the labeled quantity. Eighty-eight percent of the products were inaccurately labeled, and only 12% of the products contained a quantity of melatonin that fell within 10% of the amount on the label. Among those products that listed CBD on the label, the actual amount ranged from 104% to 118% of the declared amount.

A study of Canadian melatonin products yielded similar results. Across 16 brands, the melatonin dose ranged from 17% to 478% of that listed on the label.

Use the smallest effective dose

Since melatonin products can contain so much more of the active ingredient than their labels declare, parents and caregivers should start children on the smallest possible dose.

"Only very low doses are needed to give a big boost to the amount of melatonin that our bodies are already producing," said McQueen. "For children especially, a dose of 0.3 to 1 mg is appropriate. Those doses can also be appropriate and effective for most adults, although up to 5 mg could be used."

Manage expectations

Parents and caregivers should not expect melatonin to take effect right away, nor should they increase the dose to get faster results.

"I usually describe it as 'helping to make the attempts to sleep more successful.'" McQueen said. "Effects are seen over the course of several days or weeks as the sleep patterns improve. Even though some individuals may sense some improvement within a night or two, most won't—and we shouldn't think of using melatonin for immediate relief of insomnia."

Melatonin is not for every child

Because melatonin is a hormone produced by the pineal gland in the brain, parents should administer it judiciously. It is generally considered safe for use in younger children and in older postpubescent teenagers, but not in peripubescent adolescents.

"Melatonin should not be used in adolescents, as it is used by the body to trigger some changes associated with puberty," McQueen said.

Finally, parents should be made aware of interactions that melatonin can have with other drugs, including seizure medications, immunosuppressants, and the antidepressant fluvoxamine. ■

States continue to pass laws giving patients access to pharmacist-provided patient care services

LOREN BONNER

Pharmacists all across the nation felt a boost when a law was passed in Maryland on May 3, 2023, allowing pharmacists in the state who are practicing within their scope of practice to be reimbursed by private and public health plans.

"This is acknowledgment of what we bring to the table as pharmacists," said Jade Ranger, PharmD, co-owner of The Prescription Shoppe in Williamsburg, VA.

Maryland's new law is unique in that language in the bill covers payment from commercial insurance, public insurance, nonprofit health plans, and children's health insurance programs.

Maryland's HB 1151/SB 678, which takes effect in October 2023, will allow pharmacists to bill for any service that is within their scope of practice that health care plans cover for other providers. For example, Maryland pharmacists

Nebraska
Nebraska's LB 227 was adopted and codifies pharmacy technicians' authority to administer vaccinations under the supervision of a pharmacist.

North Dakota
North Dakota's HB 1095 was enacted and allows for the reimbursement of comprehensive medication management provided by pharmacists by health plans in the state.

Montana
Montana's HB 710 was adopted and codifies pharmacy technicians' authority to administer vaccinations under the supervision of a pharmacist. SB 112 was also recently signed into law in Montana and authorizes pharmacists to prescribe medications for conditions that do not require a new diagnosis, are minor and generally self-limiting, and can be diagnosed with a CLIA-waived test or are patient emergencies.

Wyoming
Wyoming's SF 9 was signed into law and recognizes pharmacists as health care providers within the state's Medicaid program. The new law also establishes a pathway for pharmacists to be reimbursed for their patient care services by the state's Medicaid program.

Colorado
Colorado's SB 162 makes numerous changes, including expanding pharmacy technicians' scope of practice to perform point-of-care tests under the supervision of a pharmacist and expanding reimbursement options for pharmacists for the administration of vaccinations to patients under the age of 19 years by the state Medicaid program.

Nebraska
Nebraska's LB 227 was adopted and codifies pharmacy technicians' authority to administer vaccinations under the supervision of a pharmacist.

Nevada
Nevada's AB 156 expands pharmacists' scope of practice to assess, prescribe, and dispense drugs for medication assisted treatment. In addition, SB 161 expands coverage by health plans of pharmacist-prescribed hormonal contraceptives.

New Mexico
New Mexico's SB 92 was signed into law and authorizes pharmacists to test and treat for flu, Group A *Streptococcus*, COVID-19, UTI, and other emerging public health threats via a statewide protocol. Additionally, pharmacists in New Mexico are authorized to prescribe HIV pre-/post-exposure prophylaxis (PrEP/PEP) via a statewide protocol.

Connecticut

A new law in Connecticut aims to improve access to birth control by allowing pharmacists to prescribe certain forms without requiring a doctor's visit first. The law permits pharmacists to prescribe hormonal and emergency contraceptives after completing an accredited educational training program related to the prescribing of these contraceptives.

In addition, Connecticut's SB1102 expands pharmacists' authority to administer vaccinations and codifies pharmacy technicians' authority to administer vaccinations under the supervision of a pharmacist. Additionally, the bill expands pharmacists' authority to administer point-of-care tests and prescribe and dispense HIV PrEP and PEP.

Maine

Maine's SP 158 will allow pharmacists to prescribe and dispense hormonal contraceptives to patients who previously have been issued a prescription for hormonal contraceptives.

Maine's LD 1151/SP 478 expands pharmacists' authority to administer vaccinations to patients ages 3 years and up. In addition, LD 1728/SP 692 updates state law to allow pharmacists to provide increased access to opioid antagonists other than naloxone.

New Hampshire

New Hampshire's SB35 will expand the vaccinations pharmacists are able to administer to include immunizations for respiratory syncytial virus.

New Jersey

New Jersey Governor Phil Murphy recently signed into law SB 275, which authorizes pharmacists to prescribe self-administered hormonal contraception pursuant to a standing order in accordance with protocols established by the New Jersey Board of Pharmacy and the State Board of Medical Examiners. This adds New Jersey to the list of over 20 states that have either passed similar legislation or are in the process of implementing these services.

New York

New York's A1060 will allow pharmacists to dispense hormonal contraceptives under a nonpatient specific order written by a physician or a certified nurse practitioner.

Vermont

Vermont's H 305 was passed by the Vermont House and Senate. The bill made updates to specify pharmacists' authority to test and treat for acute ailments and pharmacy technicians' authority to administer vaccinations under the supervision of a pharmacist. Governor Phil Scott vetoed the bill on June 1, 2023, and the veto was overridden June 20, 2023.

Vermont's S 37 will allow pharmacists to prescribe emergency contraceptives pursuant to a state protocol.

Illinois

Illinois' HB 559 authorizes pharmacists to test and treat for COVID-19, test for influenza, COVID-19, and other emerging and existing public health threats, and provides coverage for these services by health plans in the state. Additionally, the bill expands pharmacists' authority to administer COVID-19 and flu vaccinations to patients 7 years and older.

The Illinois Department of Healthcare and Family Services, which administers the state's Medicaid program, recently received approval from CMS to allow pharmacists to bill for services associated with the prescribing of HIV PrEP and PEP. CMS' approval comes after the passage of HB 4430 in 2022, which expanded pharmacists' ability to furnish HIV PrEP and PEP through a standing order and required coverage of these services by public and private health plans in the state.

Indiana

Indiana's HB 1568 will allow pharmacists to prescribe and dispense hormonal contraceptives under a standing order and provides coverage for these services by the state Medicaid program.

Maryland

Maryland's HB 693/SB 647 was signed into law and expands pharmacy technicians' authority to administer certain vaccinations under the supervision of a pharmacist.

As described in the introduction of this story, Maryland's HB 1151/SB 678 was signed into law and allows for the reimbursement of services provided by pharmacists practicing within their scope of practice by private and public health plans in the state.

Virginia

Virginia's SB1538 was adopted and recognizes pharmacists as providers within the state Medicaid program and requires Medicaid to cover pharmacists' patient care services.

Virginia's SB948/HB2274 was signed into law and authorizes pharmacists to test and treat for group A *Streptococcus*, flu, COVID-19, and UTI via a statewide protocol.

Arkansas

Arkansas passed HB 1007 which expands pharmacists' authority to prescribe HIV PrEP/PEP via a statewide protocol.

Georgia

Georgia's HB 440 was signed into law and expands pharmacists' scope of practice to allow pharmacists to dispense glucagon pursuant to a prescriber protocol.

Georgia's HB 416 was adopted and codifies pharmacy technicians' authority to administer vaccinations under the supervision of a pharmacist.

North Carolina

CMS recently approved North Carolina Medicaid's request to add pharmacists' services related to prescribing COVID-19 therapeutics, including Paxlovid (Pfizer) prescribing. These services are covered beginning February 1, 2023, through at least 12 months after the end of the public health emergency.

PBM reform state by state

States have also been busy this year enacting legislation to reform PBMs and health plans. More than 18 states have done so since the beginning of 2023. Some recent examples as of June 26, 2023, include

- Louisiana's HB 548 which will create protections from PBMs for contract pharmacies and covered entities in the 340B program.
- Nevada's AB 434 which establishes protections for contract pharmacies and covered entities in the 340B program from discriminatory practices by PBMs.
- Oregon's SB 608 which requires that the state Medicaid program conduct a survey every three years to determine the cost of dispensing and update dispensing fees based on the results of the survey.
- Texas' HB 1647 which was recently signed into law and prohibits white bagging mandates by health plans and PBMs related to clinician-administered drugs.

Federal agencies, including CMS, as well as federal bills also seek to address PBM reform in various ways. Keep an eye on APhA's Legislative and Regulatory Update newsletter for the latest. ■

had a scope of practice change that allowed them to prescribe nicotine replacement therapy, but without payment for services covered in the bill. Now with this recent legislation, pharmacists can bill for the counseling and screening involved for the nicotine replacement therapy service.

Maryland's new law is unique in that language in the bill covers payment from commercial insurance, public insurance, nonprofit health plans, and children's health insurance programs.

"It was truly vetted by the insurance administration to make implementation as smooth as possible," said Aliyah Horton, executive director of the Maryland Pharmacists Association.

She said they were happy to receive support for the bill from physician practices and federally qualified health centers.

"They stated they could increase the use of pharmacist's expertise in their practices and hire more pharmacists because there was a funding mechanism to cover their services," Horton said. "This creates fantastic opportunities for new graduates, those seasoned in certain practice areas, and for ramping up implementation of scope of practice changes that have been advanced in recent years."

"For so long it has always been pharmacists behind counters—and there is nothing wrong with that—it is just refreshing to see that we are moving beyond the counter."

Horton said relationships, communications, and data were key in getting the bill passed.

"Many of our members have relationships with legislators. The legislators know the role and impact specific pharmacists and pharmacies have in their communities," she said. "Legislators are also keenly aware of the challenges pharmacies have with PBMs and reimbursements. This bill supports more access to pharmacists and creates a payment opportunity that is largely beyond the scope of PBMs. Our elected leaders do not want to lose more pharmacies in their communities."

Besides this win for pharmacists in Maryland, this year has brought an abundance of legislative victories to pharmacists—and their patients—in many other states. Within these pages is a roundup of laws which advance pharmacists' scope of practice and payment for services that have passed in states so far in 2023.

"There are so many clinical services pharmacists can bring into the fold," said Ranger. "For so long it has always been pharmacists behind counters—and there is nothing wrong with that. It is just refreshing to see that we are moving beyond the counter. We need to continue the momentum." ■

What could the future of food allergy treatment look like?

Clarissa Chan, PharmD

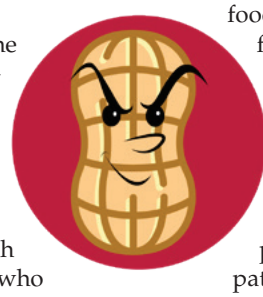
Palforzia (peanut allergen powder-dnfp–Aimmune Therapeutics), which was FDA-approved in 2020, has been giving people with peanut allergies protection from severe reactions. By using novel, medical-grade peanut (Arachis hypogaea) powder, Palforzia ensures consistent, accurate dosing of the allergic protein following strict treatment protocols.

Pharmacy Today asked Erin Malawer, executive director of AllergyStrong and cofounder of the Food Allergy Collaborative, to discuss Palforzia and its impacts on the future of patients with peanut and other food allergies.

Future horizons

According to FDA, Palforzia is both safe and effective for desensitizing patients to peanuts.

"Palforzia offers patients and their caregivers relief in knowing they have some level of protection in reducing the incidence and severity from accidental exposure to peanuts, which is the primary goal of OIT [oral immunotherapy]," said Malawer. "We call this accidental exposure 'bite-safe' protection."



Since Palforzia is the only FDA-approved treatment for peanut allergies, insurance companies are more likely to cover costs associated with Palforzia versus off-the-shelf OIT. Coverage extends the reach of treatment to patients who otherwise cannot afford it, Malawer said.

Palforzia is changing the landscape for those living with food allergies, said Malawer. "It's the gateway for future food allergy treatment approval," she said. "Those with food allergies need more treatment options to fit the allergies, stage of life, and lifestyle they live with, and FDA's approval of Palforzia is the first step in that direction."

In the pipeline

Researchers are studying many different treatment avenues to lessen the burden of food allergies, including approaches through the microbiome and skin, various oral immunotherapies (oral, oral mucosal, sublingual), and even injectable peanut vaccines.

Patients have expressed interest in therapies that go beyond the peanut and those with long-lasting results. The future of food allergy treatment is encouraging, but a cure is still needed, Malawer said.

"Epicutaneous immunotherapy—also known as the 'peanut patch'—has shown promising results recently," Malawer said. "Worn as a patch, patients absorb peanut protein through the skin and build tolerance that way."

Additionally, developing a low level of tolerance may allow some patients' food purchasing to include food with precautionary labels like "made in a facility with…" or "may contain," she said.

Potential concerns

Malawer worries that parents, caregivers, and patients may think that undergoing OIT will allow them to freely eat their allergen upon completion of treatment. Health care providers and advocacy organizations need to clearly and consistently communicate and establish realistic expectations about treatment end goals and what "bite-safe protection" really means, said Malawer.

Palforzia competes with off-the-shelf OIT. While Palforzia offers a measured and regulated path to bring patients to bite-safe levels of protection, it must also provide revenue to health care practices. "Some physicians claim they can achieve higher levels of tolerance with off-the-shelf OIT and cite the cost of Palforzia as a hindrance," Malawer said.

How pharmacists can inform patients

As pharmacists process epinephrine autoinjector prescriptions, they may discover their patients have food allergies. It is important for pharmacists to collaborate with allergists and to counsel patients about Palforzia and its use, Malawer said.

"Correct use of this product is critical, as mistakes could lead to anaphylaxis," said Malawer. "Pharmacists' careful review of protocols and reinforcing providers' instructions will help ensure Palforzia is dosed properly."

Pharmacists can also help patients think through their food allergy needs as they undergo OIT. They can make sure patients have a current epinephrine prescription, and remind them to keep it at room temperature and to carry a set with them at all times, Malawer said.

Other considerations since the launch of Palforzia

Many people with multiple food allergies await treatment, risking accidental food allergy reaction if exposed to their allergen.

"It will be important to develop a standardized, Palforzia-like product for other allergens, as peanuts are only one of the nine most common allergens," said Malawer. "We also need treatments that are effective at protecting adults with other food allergies, as they comprise about 26 million of 32 million Americans living with food allergies today."

Nasal epinephrine is presently pending FDA approval. Since epinephrine is currently only available by intramuscular injection, many patients fail to fill their prescription or use their epinephrine autoinjector prescriptions when needed due to their fear of needles, Malawer said.

"Nasal epinephrine delivery devices will be smaller and easier to carry (and needle-free), reducing the barrier to use in a timely way. This will ultimately save lives," said Malawer. ■

Increasing use of prescription digital therapeutics

Loren Bonner

Pharmacists and other clinicians are going to see digital therapeutics (DTx) and prescription digital therapeutics (PDTs) affect pharmacotherapy in the coming years, said Timothy Aungst, PharmD, lead author of a recent paper about PDTs published April 2, 2023, in *JAPhA*.

DTx are evidence-based, FDA-authorized software to treat or manage medical conditions and are available either via prescription or as nonprescription products. DTx that require clinician initiation and oversight are called prescription DTx (PDTs).

"We will see an increasing number of changes to conditions due to new digital health data that will help adjust therapy in real time, either with a medication or through adjunctive treatments delivered digitally," said Aungst, who is an associate professor of pharmacy practice at the Massachusetts College of Pharmacy and Health Sciences.

"That is where health care is going," Aungst said.

Pharmacists, in turn, will have to understand how this technology affects a patient's medications.

In the *JAPhA* commentary, Aungst and coauthor Gigi Shafai, PharmD, said that pharmacists will need further education and training on digital health tools such as PDTs, since they may be involved in direct dispensing or support.

"There isn't much information in the published literature about DTx and PDTs for pharmacists to read about at this time," said Aungst. "Most published literature is targeted toward payers and health care decision makers, and yet very little toward helping the majority of pharmacists understand what new technological developments are going on in health care."

Aungst said they wanted to create a resource that any pharmacist could "pick up and understand" if they were new to the topic.

A scenario

DTx and PDTs have unique mechanisms of action and are expanding treatment options beyond traditional pharmacotherapy. They may be implemented on their own or used in combination with a drug and in some cases, may be the only treatment option for a particular disease state.

As an example, Aungst said health care will move toward a point where insulin will be adjusted for patients in real time. In this scenario, a patient would pick up their pen or vial insulin product and go home. At home, their continuous glucose monitoring (CGM) data would interpret their blood glucose in real time. Then, a DTx/PDT product could take that data and tell the patient to adjust therapy based on the results.

"What if the patient now needs more or less due to the platform adjusting therapy faster than traditionally seen in practice? How does that impact billing or payment and what is dispensed, just at the medication dispensing level?" Aungst said.

In that case, "we start seeing some things really change in the patient care approach," said Aungst.

While this doesn't address clinical outcomes or medication safety concerns, the concept can be applied to many other conditions.

"We will see an increasing number of changes to conditions due to new digital health data that will help adjust therapy in real time."

What can pharmacists do now?

Although digital health won't become

FDA-authorized PDTs[a]

PDT product	Company	Indication/therapeutic area	Mechanism of action
reSET	Pear Therapeutics	Substance use disorder	CBT/CM on mobile devices
reSET-O	Pear Therapeutics	Opioid use disorder	CBT/CM on mobile devices
Somryst	Pear Therapeutics	Chronic insomnia	CBT for chronic insomnia on mobile devices
NightWare	NightWare	PTSD-driven traumatic nightmares	AI software paired with Apple Watch
EndeavorRx	Akili	ADHD	Adaptive algorithms (Selective Stimulus Management) delivered via video game on mobile devices
Parallel	Mahana	IBS	CBT on mobile devices
RelieVRx	AppliedVR	Chronic lower back pain	Behavioral therapy sessions delivered on VR headset
Luminopia One	Luminopia	Amblyopia in children aged 4–7 years	Videos delivered on VR headset
Regulora	metaMe Health	Abdominal pain associated with IBS in adults	Hypnotherapy delivered on mobile devices
Freespira	Freespira	Panic disorder/PTSD symptom management	Software and breathing sensor paired with mobile devices

Abbreviations: AI, artificial intelligence; CBT, cognitive behavioral therapy; CM, contingency management; IBS, irritable bowel syndrome; PDT, prescription digital therapeutics; PTSD, post-traumatic stress disorder; VR, virtual reality.
[a] As of March 2023.
Source: Shafai and Aungst. *JAPhA*. Published online April 2, 2023.

widely used overnight, Aungst said steady changes will be noticeable.

"We create new technology, generate evidence, get regulatory approval, and clinical guidelines adopted. But it can take years," said Aungst. "I look at diabetes and CGM and how we are adopting new terms in diabetes care due to that technology adoption. It took a lot of years, but to facilitate just reading CGM data and then implementing the data into practice is where we see novel technologies like DTx/PDTs adopt them to transform how we conduct care."

He envisions a closed-loop system for insulin, with a CGM plus DTx/PDT plus insulin delivery device all working together.

"Systems for other conditions like hypertension are sure to follow," said Aungst. "And I think this really changes up how patients, providers, and pharmacists all look at disease management going forward."

Aungst said pharmacists can expect to find more material coming out on this topic—in many publications as well as in continuing education courses. ■

APhA's Pharmacy Library page on digital health includes resources on health/technology professional organizations and centers, conferences/events, publications, article, blogs, podcasts, and practice tools/resources.

Available at https://pharmacylibrary.com/digitalhealth

Semaglutide shortage gives rise to unauthorized products

Sonya Collins

Fueled by celebrity endorsements, the increasing popularity of semaglutide injection (Wegovy—Novo Nordisk and Ozempic—Novo Nordisk) as a highly effective weight loss drug helped land it on FDA's shortage list last year, where it remains today.

In the event of an FDA-recognized shortage, 503A compounding pharmacies are authorized to produce "essential copies" of the drug for patients who have a prescription. However, some facilities may be producing unauthorized "look-alikes." Drugmaker NovoNordisk and some state boards of pharmacy have begun to issue warnings and take action against these alleged bad actors.

The controversy

Federal regulations allow 503A compounding facilities to use active pharmaceutical ingredients to make compounded versions of drugs that are in FDA-recognized shortage for patient-specific prescriptions. But FDA has received reports of adverse reactions with compounded semaglutide. It has also received reports of compounded products containing semaglutide salts, which may or may not be behind the adverse reactions.

"Salt forms, such as semaglutide sodium or semaglutide acetate, may have different aqueous solubility than that of the base form of semaglutide," said Jasmine Gonzalvo, PharmD, a clinical professor in the College of Pharmacy and director of the Center for Health, Equity and Innovation at Purdue University in Indiana. "These differences in solubility could affect the rate and extent of absorption of the compounded formulations, particularly when combined with other ingredients. The safety and effectiveness risks associated with these differences are unknown at this time."

In response to reports of salt-based compounded semaglutide products, FDA's F. Gail Bromel, RPh, JD, director of the Center for Drug Evaluation and Research Office of Compounding Quality and Compliance, wrote a letter to the executive director of the National Association of Boards of Pharmacy. She wrote, "We also wish to ensure [the executive director is] aware that the active pharmaceutical ingredient in Wegovy and Ozempic is semaglutide in its base form. We are aware that in some cases compounders may be using salt forms of semaglutide, including semaglutide sodium and semaglutide acetate. We are not aware of any basis for compounding a drug using these semaglutide salts that would meet federal law requirements that limit the types of active ingredients that can be used in compounding."

Some state boards of pharmacy have released statements or issued warnings reiterating the FDA's position on semaglutide salts. NovoNordisk has started legal action against some facilities, including med spas and clinics, believed to be producing unauthorized semaglutide products.

Some facilities claim to have received cease-and-desist letters from the drugmaker, though they are in compliance with FDA regulations.

"Any compounding pharmacies who have received warnings from the drug manufacturer should seek legal counsel," Gonzalvo said.

Looking ahead

While Novo Nordisk is currently producing and shipping all dose strengths of Wegovy, prescribing continues to outpace production. According to its website, Novo Nordisk anticipates it will be unable to fully meet demand for 0.25 mg, 0.5 mg, and 1 mg dose strengths through September 2023. It does not expect any interruptions in the supply of its 1.7 mg and 2.4 mg products.

Until supply once again surpasses patient and provider demand, Gonzalvo said that for pharmacists compounding semaglutide, legal ramifications should be prioritized.

"Safety risks can likely be minimized if patients get their prescriptions filled at state-licensed compounding pharmacies that are able to obtain the base form of semaglutide from FDA-registered facilities."

In the face of safety concerns about compounded semaglutide, community pharmacists who are unable to fill patient prescriptions for semaglutide as written, might explore alternative strategies with prescribers, such as

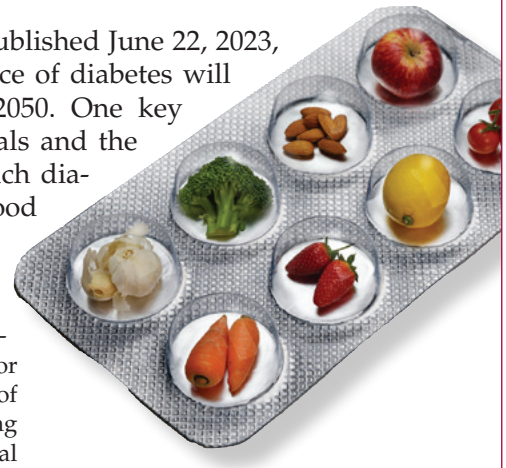
- Using one to two doses of available lower doses to achieve a higher prescribed dose
- Changing to another GLP-1 agonist
- Prescribing another medication class for weight loss

"Currently, insufficient data are available to support the safe or effective use of compounded formulations of GLP-1 agonists," said Gonzalvo. "Safety risks can likely be minimized if patients get their prescriptions filled at state-licensed compounding pharmacies that are able to obtain the base form of semaglutide from FDA-registered facilities, ensure sterility during the compounding process, and avoid the addition of other ingredients with unknown potential for interactions." ■

Food as medicine is real

Mickie Cathers

According to a new study published June 22, 2023, in the *Lancet*, the prevalence of diabetes will increase 60% worldwide by 2050. One key to the puzzle is how individuals and the health care community approach diabetes and how that relates to food and nutrition.



"Poor nutrition has surpassed smoking as a main risk factor for preventable chronic disease," said Taylor Newman, PhD, RD, LD, director of nutrition at Kroger Health, during a session at the 2023 APhA Annual Meeting & Exposition in Phoenix. Poor nutrition is one of four main risk factors for preventable chronic diseases and is the leading risk factor for deaths worldwide. Heart disease, stroke, and T2D have reached $50 billion a year in health care costs.

Improving a patient's health starts at the grocery store, where decisions are first made about what to bring home.

Nutrition security is tied to health equity and is an essential social determinant of health (SDOH) that exists everywhere, even in affluent neighborhoods. "If you are obese and overweight, you are in nutrition insecurity," said Jim Kirby, PharmD, BCPS, FAPhA, chief commercial officer at Kroger Health during the APhA2023 session.

Grocery store as a unique health care destination

Improving a patient's health starts at the grocery store, where decisions are first made about what to bring home, said Kirby. "How often do you go to the doctor? How often do you go to the grocery store?" asked Kirby.

Grocery stores are frequent touch points with a wide geographic footprint and may offer accessibility, convenience, and in-store registered dieticians. "This is an opportunity for collaboration and interprofessional care between pharmacists and dieticians," said Kirby. He encourages pharmacists to advocate for dieticians. "They are your teammates. They help you take care of your patients," said Kirby.

Kroger partnered with the University of Cincinnati on a randomized controlled trial evaluating an individualized supermarket- and web-based intervention targeting nutrition (SuperWIN). The goal was CV risk reduction and adherence to the dietary approaches to stop hypertension (DASH) diet. The results of SuperWIN were published in *Nature* on December 1, 2022, and revealed clinically relevant and meaningful improvement in participants' DASH score from baseline after 2 weeks which persisted to the study close at 3 months.

In the study, in-aisle education significantly increased adherence to the DASH dietary pattern compared to traditional nutrition counseling alone.

Kroger Health offers a suite of tools and resources helping people navigate healthy eating including the OptUP nutrition rating system. The OptUP app is a consumer tool that gamifies healthier food shopping and allows shoppers to track their progress.

"Patients can share their OptUP score with their pharmacist or physician to open up the conversation," said Kirby. "It's easier to have a discussion around reducing BP than just saying 'lose weight, eat more fruits and veggies.'"

Pharmacists are uniquely situated to play an important interdisciplinary role in nutrition care. As pharmacists are more accessible to patients than physicians and can meet patients where they are in their community, they can start this conversation with their patients and engage SDOH screening. ■

Instacart and Walmart roll out 'food as medicine' programs

Instacart recently unveiled a program that includes a suite of tools enabling health care providers to prescribe food in the same way they would medications. Instacart Health is a "virtual food pharmacy" increasing access to healthy food, providing tools for nutritious grocery shopping, and offering a new platform for health care providers to recommend and order groceries for patients, which would be useful for a patient who has just been discharged from the hospital or otherwise encounters barriers to getting to the store. "We've seen firsthand via independent and partner research studies that online grocery delivery helps people get access to fresh food, adopt healthier eating habits, save time, manage their budgets and eliminate transportation and mobility barriers to nutrition," said Instacart CEO Fidji Simo in a company blog post.

Walmart has also added an online and in-app platform allowing customers to "shop-by-diet" and determine if products meet their health criteria needs such as diets, allergens, interactions with medication, and medical conditions.

APhA offers a resource for building partnerships to expand access to valuable patient care services available at pharmacist.com/Practice/Practice-Resources/Team-based-Partnerships.

PHARMACISTS' TOP SELF-CA

Pharmacy Today proudly presents APhA's Self-Care Product Survey. Conducted by BrandSpark/Newsweek International using a scientifically valid methodology, the survey determines those nonprescription products most often recommended by pharmacists in the United States to consumers.

The winners were selected based on a survey of 1,716 pharmacists practicing in the United States who gave their unaided write-in opinions on which brands they'd recommend to patients in 86 categories. The highest share of citations as Most Trusted in the category determined the winner. If the margin of citation share between the leading brands did not exceed the estimate of sampling error at 90% statistical confidence, a tie was declared. Duplicate numbers represent a tie.

Please also see APhA's *Handbook of Nonprescription Drugs*, the definitive source of professional information about OTC products. The *Handbook* is available online at PharmacyLibrary.com or in print in the bookstore at www.pharmacist.com.

Cough, cold, and allergy

Adult allergic reaction treatment

Benadryl.....1

Adult seasonal allergy relief

Zyrtec.....1
Claritin.....2
Allegra.....3

Cough lozenges

Halls.....1
Cepacol.....2
Ricola.....2

PICKS OF THE RE PRODUCTS

Cough, cold, and flu multisymptom relief
Vicks Dayquil/Nyquil....1
Mucinex....2
Robitussin....2
Tylenol....2

Liquid cough expectorant
Robitussin....1
Mucinex....2

Liquid cough suppressant
Delsym....1
Robitussin....2

Nasal decongestant spray
Afrin....1
Flonase....2

Natural cold remedy
Zicam....1

Sinus rinse
NeilMed....1

Sore throat lozenges
Cepacol....1
Halls....2
Chloraseptic....3

Vapor therapy
Vicks Vapo....1

Diagnostics

Blood glucose monitors
OneTouch....1
FreeStyle....2
Accu-Check....3

Blood pressure monitors
Omron....1

Nontouch digital thermometer
Braun....1
Vicks....2

Ears and eyes

Adult earache relief
Similasan....1
Debrox....2
Hyland's Naturals....2

Contact lens solution
Bausch + Lomb....1
OPTI-FREE Puremoist....2

Eye drops for pink eye
Similasan....1
Visine....2

Eye vitamin
PreserVision....1
Ocuvite....2

Multisymptom eye drops
Visine....1
Systane....2

Family planning

Condom
Trojan 1

Pregnancy test
Clearblue .....
First Response 1
e.p.t. 2

First aid

Bandages
Band-Aid 1

Burn treatment and relief
Neosporin 1

Sunburn relief
Solarcaine 1
Banana Boat 2

Gastrointestinal

Diarrhea relief
Imodium 1

Fiber supplement
Metamucil 1
Benefiber 2

Gas relief
Gas-X 1

Heartburn relief
Tums 1
Pepcid 2

Hemorrhoid relief
Preparation H 1

Laxative
Dulcolax 1
MiraLAX 2

Nausea treatment/Relief
Dramamine-N 1
Emetrol 1
Pepto Bismol 2

Stool softener
Colace 1
Dulcolax 2

Upset stomach relief
Pepto Bismol 1
Tums 2

Oral care

Cold sore relief
Abreva 1

Dry mouth relief
Biotene 1

Oral pain relief
Orajel 1
Tylenol 2

Pain and inflammation

Back pain relief
Advil 1
Aleve 1
Tylenol 2

Rapid headache relief
Excedrin 1
Tylenol 2
Advil 3

Rapid migraine relief
Excedrin 1

Pediatrics

Children's allergic reaction treatments
Children's Benadryl....1
Children's Zyrtec....2

Children's cold relief
Children's Dimetap....1
Children's Tylenol....2
Children's Robitussin....3
Mucinex Children's....3

Children's cough relief
Children's Delsym....1
Children's Robitussin....1
Mucinex Children's....2

Children's cough/ Cold multisymptom relief
Children's Dimetapp....1
Children's Robitussin....1
Mucinex Children's....2
Children's Tylenol....3

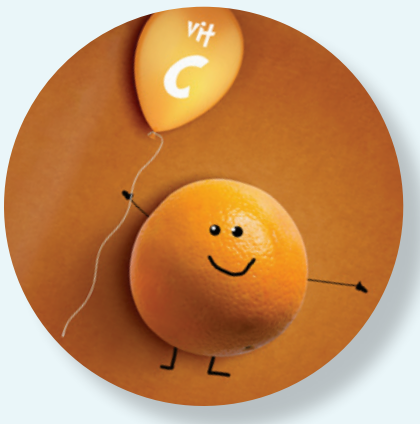
Children's earache relief
Similasan....1
Hyland's Naturals....2
Children's Tylenol....3

Children's multivitamin
Flintstones....1
Centrum Kids....2

Children's seasonal allergies
Children's Claritin....1
Children's Zyrtec....1

Supplements

Adult multivitamin
Centrum....1
One A Day....2



Greens powder supplement
AG1....1

Immune system booster
Emergen-C....1
Airborne....2

Joint supplement
Osteo Bi-Flex....1

Letter vitamins
Nature Made....1
Centrum....2
Nature's Bounty....2

Meal replacements
Ensure....1
BOOST....2

Melatonin supplements
Nature Made....1
NATROL....2

Memory support supplement
Prevagen....1

Nutritional drinks
Ensure....1
BOOST....2

Weight loss supplement
alli....1

Topicals

Acne treatment
Differin....1
Neutrogena....2
Clearasil....3

Adult sunscreen
Neutrogena....1
Coppertone....2
Banana Boat....3

Antifungal treatment
Lotrimin....1
Lamisil....2

Eczema relief
Aveeno....1
Eucerin....1
Cortizone 10....2
CeraVe....3

Hot/Cold topical pain relief
Icy Hot....1
BIOFREEZE....2

Lice treatment
Nix....1
RID....2

Medicated topical pain relief
Voltaren....1
Aspercreme....2

Scar and stretch mark treatment
Mederma....1

Women's health

Menstrual relief
Midol....1
Pamprin....2
Advil....3

Vaginal lubricant
K-Y....1
ASTROGLIDE....2
Replens....2

Yeast infection treatment
Monistat....1

Other

Incontinence products
Depend....1
Poise....2

Shampoo for severe dandruff
Head & Shoulders....1
Selsun Blue....2
Nizoral....3

Sleeping aid
Unisom....1
Benadryl....2
Vicks ZzzQuil....3

Smoking cessation
Nicorette....1
NicoDerm....2

Potential pharmacy responsibility for long-term effects of short-term opioid use

David B. Brushwood, BSPharm, JD

Many opioid-related legal cases are currently being pursued against pharmacies, alleging that a patient's brief period of opioid use years ago caused the patient to become addicted to opioids and that the dispensing pharmacy should be held legally liable for causing the patient's overdose death years later. An Ohio appellate court recently explained why this theory of liability could be legally maintainable.

Background

A high school football player injured his shoulder during a game, and he required surgery. His physician prescribed opioid medication once prior to the surgery and 4 times following the surgery, all within a period of less than 2 months in late 2009. The court indicated that the pharmacy dispensed "260 opioids" to the patient during this timeframe. The patient allegedly "became addicted to drugs based on the initial opioid pills." The patient "entered rehabilitation five times to treat his drug addiction." However, despite periods of sobriety, he overdosed on fentanyl and oxycodone and died in the fall of 2017.

The patient's estate sued the pharmacy, contending that the "over dispensing of medication to the decedent caused him to become addicted to opioids and ultimately overdose."

A physician expert witness, who was qualified as a pain and addiction specialist, testified that "there was a causal connection between the prescribed opioids in 2009, the decedent's diagnosis of opioid use disorder, and untimely death in 2017."

The trial court concluded that the estate "could not demonstrate that [the pharmacy's] actions were the proximate cause of the decedent's death." The trial court ruled that the expert's opinion was "speculative, and based on assumptions, not facts in the record."

The case against the pharmacy was dismissed, and the patient's estate appealed.

Rationale

The appellate court reviewed evidence presented by the pharmacy concerning the pharmacy's 2009 policy for pharmacist review of duplicate controlled substance prescriptions. The policy indicated that over-prescribing of opioids would be flagged by the pharmacy computer, bringing the problem to the attention of the dispensing pharmacist. However, the court noted that there was "no testimony provided that demonstrated [the pharmacy's] policy of flagging a duplicate prescription occurred even if it was designed to do so." The pharmacy's electronic record-keeping system had been purged of any records from 2009.

The court acknowledged that "the period between the dispensing of the drugs and the decedent's overdose is significant."

The appellate court also noted that the patient's opioid prescriptions maintained on file did not show that any telephone calls were made by a pharmacist to the prescriber.

The court acknowledged that "the period between the dispensing of the drugs and the decedent's overdose is significant." However, the court concluded that "addiction is a 'long-term, chronic, and relapsing disease' that is complex to evaluate in this context."

The dismissal of the case against the pharmacy was reversed. The case was remanded back to the trial court for further proceedings. The outcome of the case is yet to be determined. The plausibility of the estate's legal argument has been judicially recognized.

Takeaways

This judicial ruling is significant for several reasons:

- An allegation that five opioid prescriptions dispensed over a 2-month period may be the legal cause of a patient's death eight years later can be legally feasible.
- Simply because a pharmacy's policy from years ago required that a particular action be taken by a pharmacist does not support a legal conclusion that the action was taken at that time.
- If there is no written notation on an opioid prescription, then an expert witness may be allowed to speculate that the prescriber was not contacted by a pharmacist.
- Although concerns for the effects of opioid use disorder have expanded over time, judicial rulings may reflect perspectives of today rather than perspectives from the time care was provided.

These observations suggest that effective pharmacy risk management programs must anticipate judgments that will be made years in the future. Pharmacies must create enduring records that will support future judicial evaluations of decisions made today. ■

Inpatient*Insights*

Do corticosteroids improve outcomes for adults with septic shock?

Although corticosteroids have been used as adjunctive therapy for septic shock for more than 50 years, uncertainty persists about the effects of these medications on mortality. Previous trials and study-level meta-analyses have failed to resolve the questions regarding the role of corticosteroids in the management of patients with septic shock.

A recent patient-level meta-analysis published on May 22, 2023, in *NEJM Evidence* assessed the effect of hydrocortisone versus usual care on 90-day mortality, secondary clinical outcomes, and adverse effects and compared the effects of hydrocortisone across prespecified patient subgroups.

The researchers pooled individual patient data from septic shock trials that investigated the adjunctive use of I.V. hydrocortisone.

The primary outcome was 90-day all-cause mortality across predefined subgroups. Secondary outcomes included mortality at ICU and hospital discharge at 28 and 180 days, and the number of vasopressor-, ventilator-, and organ failure–free days. Adverse events included superinfection, muscle weakness, hyperglycemia, hypernatremia, and gastroduodenal bleeding.

Of 24 eligible trials, 17 trials provided individual patient data, and 7 trials (with a total of 5,929 patients) provided 90-day mortality data. The patient-level meta-analysis of hydrocortisone for patients with septic shock found that hydrocortisone was not associated with reduced risk of 90-day all-cause mortality. Further, the effects of hydrocortisone on 90-day all-cause mortality did not differ significantly between continuous versus bolus administration, a fixed-duration versus vasopressor dependency–guided administration, or between discontinuation with tapering versus without tapering.

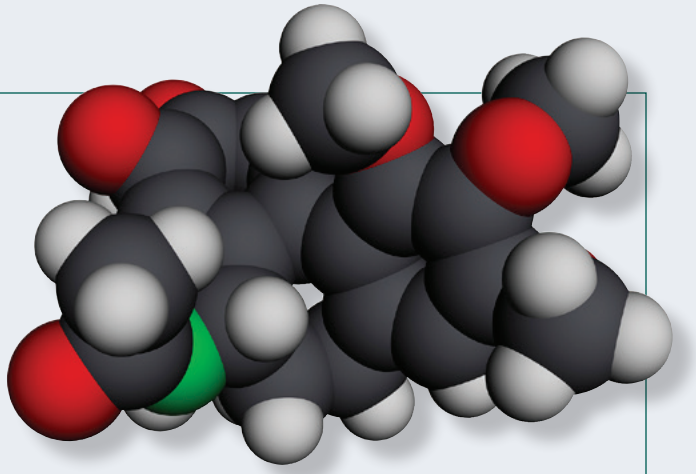
Hydrocortisone may be associated with a decreased risk of ICU mortality and with increased vasopressor-free days but may not be associated with reduced mortality at 28 days, 180 days, and hospital discharge. Hydrocortisone may be associated with an increased risk of muscle weakness. ■

Risk associated with the use of amiodarone with anticoagulants in patients with AFib

Amiodarone, the most effective antiarrhythmic drug prescribed to patients with AFib, is known to inhibit elimination of apixaban and rivaroxaban, thus possibly increasing anticoagulant-related risk for bleeding. Researchers at the Vanderbilt University School of Medicine conducted a retrospective cohort study to compare risk for bleeding-related hospitalizations during treatment with amiodarone versus flecainide or sotalol, antiarrhythmic drugs that do not inhibit these anticoagulants' elimination.

The study, published in the June 2023 issue of *Annals of Internal Medicine,* included over 90,000 Medicare beneficiaries aged 65 or older with AFib who began apixaban or rivaroxaban anticoagulant use between January 1, 2012, and November 30, 2018, and were subsequently treated with either amiodarone or with flecainide or sotalol. The primary outcome was time to event for bleeding-related hospitalizations and ischemic stroke.

Results of the study indicated that risk for bleeding-related hospitalizations increased significantly with amiodarone use compared with use of flecainide or sotalol (57 vs. 39 events per 1,000 person-years). There was no significant association with stroke or systemic embolism. ■



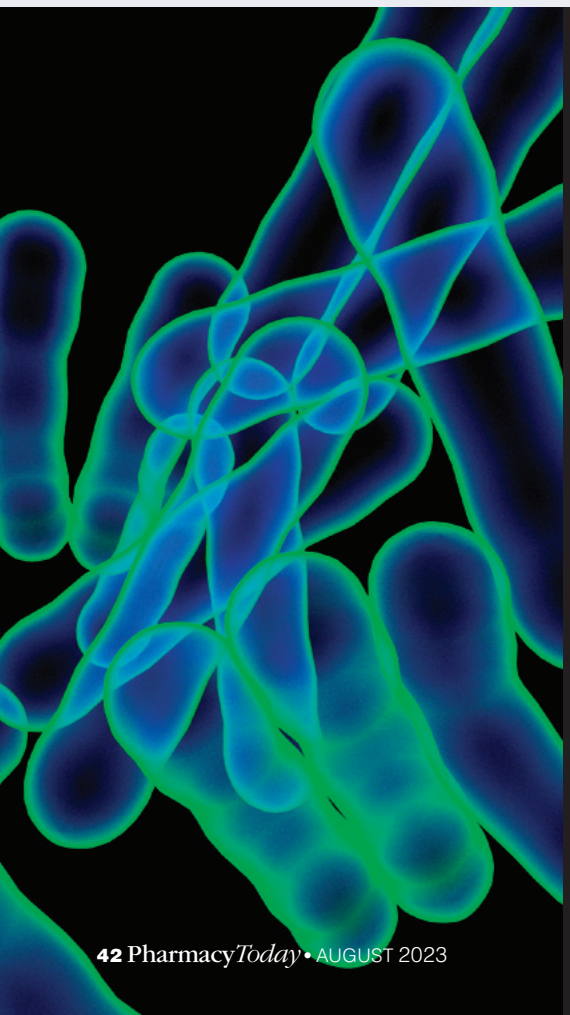
Low-dose colchicine may reduce need for knee and hip replacements in patients with osteoporosis

Colchicine, an anti-inflammatory medication that is commonly prescribed to treat gout and pericarditis, may reduce the need for knee and hip replacements in patients with osteoporosis according to a recent study published in the June 2023 issue of *Annals of Internal Medicine*. A group of researchers in the Netherlands and Australia examined data from a 2020 trial conducted to investigate the efficacy of low-dose colchicine in patients with chronic coronary artery disease and found that colchicine reduces the need for total knee or hip replacements.

Although the study was not designed to investigate the effect of colchicine in patients with osteoporosis, the researchers postulated that because inflammation plays an important role in the development of osteoarthritis, anti-inflammatory drugs such as colchicine may slow disease progression.

The researchers used data from a randomized, controlled, double-blind trial of more than 5,000 patients in 43 medical centers in Australia and the Netherlands who received 0.5 mg daily of colchicine or placebo. The authors found that during a median follow-up period of 28.6 months, 2.5% of patients in the colchicine group received a total knee or hip replacement compared with 3.5% of patients in the placebo group.

The authors concluded that further research specifically studying colchicine therapy as a means to slow disease progression in osteoarthritis is warranted. Until then, colchicine cannot be recommended as a treatment for osteoarthritis. ■



Quantifying symptoms and reactions in patients receiving treatment for latent TB

Patients with latent TB infection—those who have no symptoms of TB and can't spread the disease, but usually have a positive TB skin or blood test—may develop active TB if they do not receive treatment. However, the recommended treatment of 3 months of weekly rifapentine plus isoniazid (3HP) can result in systemic drug reactions that may cause patients to stop treatment before the end of 12 weeks, increasing their risk for developing active TB. A recent study published in the June 15, 2023, issue of *Clinical Infectious Diseases* investigated the patterns of symptom development and evaluated factors linking systemic drug reactions and treatment discontinuation.

The researchers analyzed symptoms data in participants receiving 3HP in the Tuberculosis Trials Consortium's iAdhere study, including patterns of symptom reporting across participants from baseline and 4 visits a month apart.

Among 1,002 participants receiving 3HP, 77% of patients reported at least one symptom (i.e., headache, fatigue, nausea, dizziness, and rhinorrhea), with most resolving within 8 weeks, while 11% of patients developed systemic drug reactions, broadly defined as hypotension, hives, angioedema, acute bronchospasm, or "flu-like" symptoms. Groups with a higher risk of selective dorsal rhizotomy and discontinuation included female sex, age 45 years and older, use of concomitant medications, and potentially, a history of liver disease. Among patients experiencing systemic drug reactions, nearly half were able to complete therapy.

The authors concluded that while systemic drug reactions are relatively uncommon, understanding whether they can be predicted or prevented, and their impact on treatment completion, is critical to informing the use of 3HP in routine clinical settings. They recommended that patient and provider education should focus on differentiating severe reactions where 3HP should be stopped from minor symptoms that will resolve. ■

Antimicrobial susceptibility testing advances along with antimicrobial resistance threats

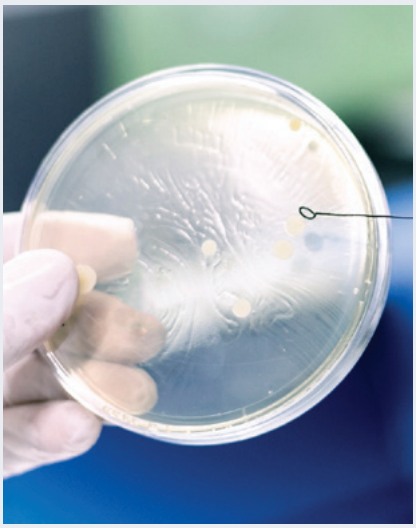
Loren Bonner

A recent paper, published February 24, 2023, in *Pharmacotherapy*, lays out the most up-to-date diagnostic stewardship—including education, communication, and interpretation—as it relates to antimicrobial susceptibility testing.

In the 14 years since the last antimicrobial susceptibility testing update was published, there has been a surge of approvals of rapid diagnostic platforms. Of course, antimicrobial resistance has only worsened during this period of time, as well.

According to lead author Elizabeth Hirsch, PharmD, the review is meant to provide clinicians with a summary of both conventional susceptibility testing methods and newer rapid methods, along with guidance on their implementation and optimization.

Hirsch and colleagues write that "antimicrobial susceptibility testing has been the cornerstone of optimal antimicrobial therapy for more than a century and will continue to play a critical role in ensuring adequate therapy for patients, as well as tracking and monitoring the spread of AMR [antimicrobial resistance]."



The only way to effectively battle antimicrobial resistance while improving patient outcomes and appropriate antimicrobial use is to take a comprehensive approach.

Defining antimicrobial susceptibility testing

According to NIH's National Library of Medicine, antimicrobial susceptibility testing (AST) is "a laboratory procedure performed by medical technologists (clinical laboratory scientists) to identify which antimicrobial regimen is specifically effective for individual patients. On a larger scale, it aids in the evaluation of treatment services provided by hospitals, clinics, and national programs for the control and prevention of infectious diseases."

The National Library of Medicine's definition also states that researchers have had to recently put continuous surveillance activities into practice for resistance patterns due to mutations in bacterial DNA.

Laboratories have many methods to chose from, including broth microdilution, agar dilution, and disk diffusion. Technological advances such as the development of commercial automated susceptibility testing platforms and the advent of rapid diagnostic tests (RDTs) have improved the rapidity, robustness, and clinical application of AST, according to authors of the review paper.

"Although many of the AST methods developed at the turn of the twentieth century are still in routine use today, the past decade has seen an explosion in new technologies including molecular and phenotypic RDTs, and more frequent updates and revisions to clinical breakpoints," the review authors write. "These rapid advances in the antimicrobial use process make strong collaborations between clinicians and microbiologists essential. Moving closer to the goal of immediate antimicrobial therapy optimization with little to no delay would benefit patients afflicted with an infectious disease syndrome."

Application to pharmacists

"The increase in new technologies, including molecular and phenotypic rapid diagnostic tests, and more frequent updates and revisions to clinical breakpoints highlight the essential need for strong collaborations between pharmacist clinicians and microbiologists," said Hirsch, who is an associate professor in the Department of Experimental and Clinical Pharmacology at the University of Minnesota College of Pharmacy.

The only way to effectively battle antimicrobial resistance while improving patient outcomes and appropriate antimicrobial use is to take a comprehensive approach, she said.

"Pharmacists are uniquely positioned to serve as these liaisons—and often serve in integral roles—among many antimicrobial stewardship programs," said Hirsch.

While the review paper is useful for infectious disease pharmacists or those working in antimicrobial stewardship, Hirsch said it's also written for noninfectious disease experts.

"[It's] especially useful for trainees and students wanting to learn more about susceptibility testing methods and diagnostic stewardship," said Hirsch. "It is highly encouraged as reading prior to any inpatient/outpatient APPE or rotation experience where a learner may need to interpret culture results and susceptibility testing in order to make recommendations surrounding antibiotic treatment or monitoring." ■

Drug expenditures expected to increase in 2023

Olivia C. Welter, PharmD

Authors of a new report published in the *American Journal of Health-System Pharmacy* (*AJHP*) predict that over the next year, overall spending on prescription drugs will rise compared to 2022.

In the new report on national trends in prescription drug expenditures and projections for 2023, new drug approvals, public health issues, and policy and legislation were all explored as factors influencing total drug expenditure.

In addition to overall spending, the report examines what drug expenditures may look like at various levels, such as within clinics or nonfederal hospitals.

2023 predictions

The report indicates that drug expenditures will likely rise in the United States by 6% to 8% overall in 2023. Clinics can anticipate spending increases in the range of 8% to 10%, and hospitals may see increases between 1% to 3%.

New drug approvals may be a contributing factor to estimated higher expenditures. FDA data show that the agency only approved 37 new drugs in 2022, which was a 26% decrease from 2021. However, the report indicates that 74 novel drugs are expected to be approved in 2023, with 22 of those anticipated to significantly impact hospitals and clinics both clinically and financially.

One drug that entered the market in 2023 is adalimumab-atto, a biosimilar of adalimumab. Adalimumab has been the top-selling drug for several years, and in 2022 it accounted for nearly 10% of all specialty drug sales. Its share of sales may decrease in 2023 due to biosimilar drugs like adalimumab-atto becoming available. In fact, FDA has approved seven other adalimumab biosimilars, but these have yet to launch for sales.

According to the report, PBMs, formulary placement, and physician preference are all factors that may influence spending on adalimumab and its biosimilars in 2023.

2022 data reveal trends

In order to provide an educated estimate on what future drug expenditures may be, the report authors reviewed 2022 spending data from the IQVIA National Sales Perspectives (NSP) database.

Most areas of the health care sector experienced increased spending on prescription drugs compared to 2021, a change driven primarily by increased drug utilization. In 2022, the total prescription expenditures in the United States was $633.5 billion.

Community pharmacies had the most costs associated with drug purchasing, accounting for 42% of total expenditures. Mail order pharmacies (28.5%), clinics (18.5%), and nonfederal hospitals (5.9%) also contributed significantly to overall spending.

Nonfederal hospitals were the only sector that decreased their pharmaceutical spending in 2022. Costs went down by 5.9%, primarily due to a 7.7% decrease in utilization.

The authors noted that the 5.9% decrease is the largest decrease since these annual reviews began in 1992. Notably, remdesivir appears to be the primary cause of this lower expenditure.

Effects of COVID-19 pandemic response

The COVID-19 pandemic fostered innovation in creating new drug products specifically to treat and prevent the disease. COVID-19 vaccines and drugs like remdesivir were administered frequently over the last several years, but use of these products has fluctuated as the severity of the pandemic has diminished.

For example, remdesivir expenditures in 2021 totaled $3.1 billion, but waned to $1.3 billion in 2022, according to the NSP database. This decrease greatly influenced hospital spending and contributed significantly to the 5.9% expenditure decrease noted for 2022.

Authors of the report used influenza vaccines as one marker in their analysis. Since vaccination is the primary management tool for flu, researchers predict that COVID-19 vaccines will be used similarly. COVID-19 vaccines moving into the commercial sector could shift spending, given that the Kaiser Family Foundation anticipates one dose will cost between $29 to $130. The authors estimate that annual expenditure on COVID-19 vaccines could be between $12.3 billion and $19.8 billion.

Clinics can anticipate spending increases in the range of 8% to 10%, and hospitals may see increases between 1% to 3%.

Public policy influence

One of the most notable pieces of health care legislation passed in 2022 was the Inflation Reduction Act (IRA). President Biden signed the IRA in an effort to lower prescription drug costs for Medicare patients.

While patient cost-sharing will decrease overall, the IRA contained various provisions that would both decrease and increase various federal expenditures.

Capping out-of-pocket spending and insulin costs, eliminating copays on vaccines under Medicare Part D, and expanding certain benefits could cause elevated spending by the government after the IRA is implemented.

Conversely, the IRA allows the federal government to negotiate drug prices and receive rebates if a medication's cost increases exceed the rate of inflation, both of which can contribute to lesser spending.

However, provisions such as price negotiation aren't expected to impact expenditures until 2026 for Medicare Part D and 2028 for Medicare Part B. ■

A minute with ...

Chris Johnson, PharmD, MEd, BCACP,
Assistant Professor, Ambulatory Care Pharmacy Specialist,
University of Arkansas for Medical Sciences College of Pharmacy,
Little Rock, AK

Member since 2011

"APhA membership has been invaluable to my pharmacy career. My membership began within the first month of pharmacy school. At first it was a way to get to know other students pharmacists, but it became an avenue through which my classmates and I could use what we were learning to benefit our community. As I've progressed through my career, connections I've developed through APhA have helped me in numerous ways. I've learned about different ways to improve my practice and community involvement, how to advocate for the profession, and how to better advise student pharmacists."

How has APhA helped you establish meaningful connections?

As a student pharmacist, membership in APhA helped me connect with my fellow student pharmacists and a community that was new to me. As a practitioner, I've been able to connect with students as a new practitioner mentor and then as an APhA–ASP Chapter advisor. APhA's Special Interest Groups (SIGs) have provided excellent opportunities to be involved in the organization and get to know pharmacists from all over the country. I've had the chance to serve with many pharmacists within the Care of Underserved Patients SIG since its inception. We've built a network that shares ideas for improving pharmacists' ability to provide care for our most vulnerable populations. It feels great to catch up with my colleagues at Annual Meetings!

How does APhA help you thrive in your everyday practice?

APhA helps me keep up to date through published resources, CPE units, BCACP credits, and various webinars that are available throughout the year. This helps provide me with up-to-date information so I'm providing the best evidence-based care I can to my patients. I find this particularly valuable in areas that are related to what I do in practice but I don't use very often for various reasons, like diabetes technology. I also have developed a network of pharmacists with different knowledge and skills I can contact with questions about different cases that come up in practice.

What excites you about the profession of pharmacy?

While there are challenges in the profession, I see a lot of potential within pharmacy. Medications and their optimal use are only getting more complex and pharmacists can make sure that patients are receiving the best medications. Pharmacy gained a lot of authority during the COVID-19 pandemic in terms of testing, treating, and prescriptive authority. Advocacy will be critical, but I'm excited to see how the profession capitalizes on these advances!

Can you share a meaningful story about a time you interacted with a patient? Perhaps a time you felt like you really made a difference for them?

I had a patient whose insulin was being managed by our clinic's pharmacy team. We kept increasing this patient's dose because his blood glucose remained high.

Eventually, we spoke with him in the clinic, and he stated that his insulin pen wasn't working. I had him walk through his injection technique with a demo pen and found that he wasn't taking both caps off his insulin needles, so he wasn't getting enough insulin. I spoke with his physician, who said that she never would've figured that out. We reset his doses, and I provided education on proper technique. The patient said that nobody'd talked to him about the pen needles before, and over time we adjusted his dose to get his blood glucose to a healthy level. ■

Advancing pharmacy practice

JAPhA, the official journal of the American Pharmacists Association, is pleased to announce a call for papers for its seventh annual special issue showcasing the scholarship of pharmacy residents. The *JAPhA* Residency Issue is the ideal forum for pharmacy residents or recent residency graduates to publish scholarship conducted during their residency training. Authors are invited to submit manuscripts in the categories of Research, Research Notes, or Advances in Pharmacy Practice.

A unique aspect of this issue is that authors will be paired with a mentor from the *JAPhA* Editorial Advisory Board to help develop their writing skills during the peer review process. **Submission deadline:** Manuscripts must be submitted at apha.us/JAPhAEM by September 15, 2023. ■

Did you hear?

JFPS 2023 is the premier event for federal pharmacists and technicians from all service branches and federal agencies.

We are thrilled to invite you to join us in Dallas on October 29–31, 2023, for an inspiring and educational gathering focused on the theme A Unified Force for Patient Care.

By working together, federal pharmacists can achieve more and make a significant impact on patient care. This year's meeting aims to break down silos and foster collaboration among federal pharmacists, all with the shared goal of providing the best possible care for patients.

Visit jfpsmeeting.pharmacist.com for updates on the meeting program, keynote speakers, registration details, and more. Together, let's make a difference in patient care and create a unified force that drives positive change in the federal pharmacy community. ■

Get involved in APhA

Immunizations have become an integral service in pharmacy. The Immunizing Pharmacists Special Interest Group (SIG) offers a way to stay up to date regarding changes in immunization recommendations as well as a way to connect with others who are involved with immunizations. APhA–APPM Immunizing Pharmacists SIG provides members valuable educational tools including the Immunization Quick Reference Guide, Travel Health Guide, and regular webinars.

"The Immunizing Pharmacists SIG is a space for pharmacists, pharmacy technicians, and student pharmacists who are interested in all aspects of immunizations; you do not need to be involved with administering vaccinations to join. The SIG helps me stay up to date with immunization-related topics and provides a place to connect with like-minded individuals," said Laura Knockel, Immunizing Pharmacists SIG coordinator. Visit www.pharmacist.com/volunteer for more information. ■

New therapeutic agents marketed in 2022: Part 2

Daniel A. Hussar, PhD, is Dean Emeritus and Remington Professor Emeritus at the Philadelphia College of Pharmacy, Philadelphia.

Part 1 (*Pharmacy Today,* March 2023) of this series on new FDA-approved therapeutic agents marketed in 2022 reviewed four new drugs: tirzepatide (Mounjaro—Lilly), daridorexant hydrochloride (Quviviq—Idorsia), tenapanor hydrochloride (Ibsrela—Ardelyx), and vonoprazan fumarate in copackaging with amoxicillin as well as amoxicillin and clarithromycin (Voquezna—Phathom).

This second part of the series includes four additional agents marketed in 2022: inclisiran sodium (Leqvio—Novartis), mavacamten (Camzyos—Bristol Myers Squibb), tezepelumab-ekko (Tezspire—AstraZeneca), and oteseconazole (Vivjoa—Mycovia).

Following the review of each new therapeutic agent, the new drug is compared with the older medication(s) with which it is most similar in properties and uses, and its advantages and disadvantages are identified. Advantages and disadvantages are identified at the time the new drug is first marketed and do not reflect approval of additional new drugs and/or changes that occur after the drug is initially marketed. The information included is primarily from the respective package inserts for the new medications.

Lipid-regulating agent

Heart disease is the leading cause of death in the United States, and high blood cholesterol concentration is an important risk factor for heart disease. Familial hypercholesterolemia is an inherited condition associated with high concentrations of low-density lipoprotein cholesterol (LDL-C).

The statins (HMG-CoA reductase inhibitors)—atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin—have been widely prescribed as the standard of therapy for reducing elevated LDL-C concentrations and the related risks of CVD. Although the statins are highly effective in reducing LDL-C concentrations, some patients do not tolerate them well, and many patients who are treated with a maximally tolerated dose of a statin still require additional lowering of LDL-C.

The cholesterol absorption inhi-bitor ezetimibe is commonly used in combination with a statin to achieve additional lowering of LDL-C; more recently, bempedoic acid (Nexletol—Esperion Therapeutics, Inc.), an adenosine triphosphate-citrate lyase inhibitor, was approved as an adjunct to diet and maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or atherosclerotic CVD (ASCVD) who required additional lowering of LDL-C.

LDL-C is removed from the blood when it binds to LDL receptors on the surface of hepatocytes. Proprotein convertase subtilisin kexin type 9 (PCSK9) is a naturally occurring enzyme that binds to LDL receptors and promotes their degradation, resulting in reduced metabolism of LDL-C and increased plasma concentrations.

Two monoclonal antibodies, alirocumab (Praluent—Regeneron Pharmaceuticals) and evolocumab (Repatha—Amgen Inc.), act as PCSK9 inhibitors and increase the number of LDL receptors available, thereby clearing LDL from the blood and resulting in a marked reduction in plasma concentrations of LDL-C that is additive to that provided with maximally tolerated doses of a statin. Although these agents are more effective than ezetimibe and bempedoic acid, they must be administered subcutaneously, whereas the latter agents are administered orally.

Inclisiran sodium also reduces the action of PCSK9, but by a different mechanism of action than alirocumab and evolocumab. Inclisiran is a small interfering RNA (siRNA) that is directed to PCSK9 messenger RNA (mRNA) and contains a covalently linked ligand consisting of three N-acetylgalactosamine residues to facilitate delivery to hepatocytes.

In hepatocytes, inclisiran utilizes the RNA interference mechanism and directs catalytic breakdown of mRNA for PCSK9. This increases LDL-C receptor recycling and expression on the hepatocyte cell surface, which increases LDL-C uptake and lowers LDL-C concentrations in the circulation. It is administered subcutaneously and is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or clinical ASCVD who require additional lowering of LDL-C.

Learning objectives

At the conclusion of this knowledge-based activity, the pharmacist will be able to

- Identify the new therapeutic agents and explain their appropriate use.
- Identify the indications and mechanisms of action of the new agents.
- Identify the most important adverse events and other risks of the new therapeutic agents.
- State the route of administration for each new drug and the most important considerations regarding dosage and administration.
- Compare the new therapeutic agents with older medications to which they are most similar in properties and/or use and identify the most important advantages and disadvantages of the new drugs.

Preassessment questions

Before participating in this activity, test your knowledge by answering the following questions. These questions will also be part of the CPE assessment.

1. Which of the following agents is administered once a day?

a. Inclisiran
b. Mavacamten
c. Tezepelumab
d. Oteseconazole

2. Which of the following agents is contraindicated in females of reproductive potential, including those who are using contraception?

a. Inclisiran
b. Mavacamten
c. Tezepelumab
d. Oteseconazole

3. Which of the following statements is correct regarding inclisiran?

a. It has been demonstrated to reduce the risk of adverse CV events.
b. It is administered intramuscularly.
c. It is administered once every 6 months during maintenance treatment.
d. Concurrent use with a moderate or strong CYP3A4 inhibitor is contraindicated.

On July 7, 2023, FDA approved an expanded labeled indication for inclisiran. It is now indicated "as an adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C)."

The effectiveness of inclisiran was initially evaluated in three placebo-controlled clinical trials that enrolled 3,457 adults who were being treated with maximally tolerated statin therapy. Two of the studies were conducted in patients with clinical ASCVD, and the other was conducted in patients with HeFH. In each of the three studies, there was a reduction in LDL-C of approximately 50% in patients treated with inclisiran compared with those receiving a placebo. Although less pronounced than the reductions in LDL-C, there were also substantial reductions in total cholesterol, non–HDL-C, and apolipoprotein B concentrations in the patients treated with inclisiran.

In addition to reducing LDL-C, statins and PCSK9 inhibitors have been demonstrated to reduce the risk of CV events such as myocardial infarction and stroke in patients with established CVD. The experience with inclisiran is much more limited and it has not been determined whether it reduces the risk of CV events.

The labeled indications for alirocumab and evolocumab include use alone in patients with primary hyperlipidemias including HeFH and as an adjunct to other LDL-C–lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH). Currently labeled indications for inclisiran include use in patients with primary hyperlipidemia, including HeFH, to reduce LDL-C.

The adverse events most commonly experienced with inclisiran in the clinical trials include injection site reaction (8%), arthralgia (5%), UTI (4%), diarrhea (4%), bronchitis (4%), pain in extremity (i.e., limbs; 3%), and dyspnea (3%). However, with the exception of injection site reactions, the incidence of these events in patients receiving a placebo was only slightly lower than in those treated with the new drug.

If used during pregnancy, inclisiran may cause adverse developmental events because of its mechanism of action to reduce cholesterol concentrations, and it should be discontinued if a patient becomes pregnant. The effectiveness and safety of inclisiran have not been established in pediatric patients, whereas evolocumab is indicated for use in patients 10 years and older.

Inclisiran is primarily metabolized by nucleases to shorter nucleotides, and approximately 16% of a dose is excreted via the kidneys. Dosage adjustment is not necessary in patients with mild, moderate, or severe renal impairment or in patients with mild or moderate hepatic impairment. It has not been studied in patients with severe hepatic impairment or end stage renal disease.

Inclisiran is administered subcutaneously into the abdomen, upper arm, or thigh. The recommended dosage, in conjunction with maximally tolerated oral statin therapy, is 284 mg initially, again at 3 months, and then every 6 months. For some patients, the long duration of action that permits administration of maintenance doses only once every 6 months will be an advantage compared with alirocumab and evolocumab, which are both administered every 2 or 4 weeks.

However, it is recommended that the new drug be administered by a health care professional, whereas alirocumab and evolocumab are usually self-administered. The new drug is supplied in single-dose prefilled syringes containing 284 mg of inclisiran sodium per 1.5 mL.

Agent for hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease, affecting at least 1 in 500 adults in

Comparison of inclisiran with alirocumab and evolocumab

Advantages

- It has a longer duration of action and is administered once every 6 months during maintenance treatment (whereas alirocumab and evolocumab are administered every 2 or 4 weeks).
- It has a unique mechanism of action (reduces the formation of PCSK9, whereas alirocumab and evolocumab inhibit action of PCSK9).

Disadvantages

- Reduction in risk of CV events has not yet been determined.
- Labeled indications are more limited.
- Effectiveness and safety in pediatric patients have not been established (compared with evolocumab, which is indicated for patients 10 years and older).
- It has not been directly compared with other LDL-C–lowering drugs in clinical studies.
- It should be administered by a health care professional (whereas alirocumab and evolocumab are usually self-administered).

the United States.

It occurs as a consequence of excessive interaction (i.e., cross-bridge formation) between two cardiac proteins (actin and myosin) and is characterized by thickening and stiffening of the left ventricle as well as a reduction in the amount of blood the left ventricle can hold and pump to the rest of the body.

Some patients with HCM may be asymptomatic and undiagnosed, but most have obstructive disease (oHCM) associated with thickening of the heart muscle, primarily the septum. Septal hypertrophy and other structural abnormalities result in narrowing of the path through which blood flows out of the heart, left ventricular outlet tract (LVOT) obstruction, the heart pumping harder to overcome the obstruction, and increased risk of worsening heart failure and death.

Symptoms of oHCM include palpitations, shortness of breath, swelling of the legs, and decreased exercise capacity.

The treatment of oHCM has involved symptom management, with a nonvasodilating beta blocker such as metoprolol usually considered as first-line treatment. In patients for whom a beta blocker is not effective or not tolerated, a nondihydropyridine calcium channel blocker (i.e., diltiazem, verapamil) has been used as an alternative. If severe symptoms persist, disopyramide has been used in combination with one of the other drugs.

Another step in symptom management is to avoid medications such as vasodilators (e.g., dihydropyridine calcium channel blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers) that may promote outflow tract obstruction. In patients with severe oHCM that is refractive to drug therapy, surgical septal reduction is often effective.

Mavacamten is a cardiac myosin inhibitor that reduces the interactions between myosin and actin, thus reducing the probability of force-producing (i.e., systolic) and residual (i.e., diastolic) cross-bridge formation, reducing LVOT obstruction, and improving cardiac filling pressures. It is the first medication that targets the underlying pathology of oHCM and is specifically indicated for oral use for the treatment of adults with symptomatic New York Heart Association (NYHA) Class II–III obstructive hypertrophic cardiomyopathy to improve functional capacity and symptoms.

The effectiveness of mavacamten was evaluated in a placebo-controlled 30-week clinical trial of 251 adults with symptomatic obstructive oHCM and a left ventricular ejection fraction (LVEF) of ≥55%. Of the trial participants, 75% were taking a beta blocker and 17% were taking a calcium channel blocker. However, patients on dual therapy with a beta blocker and calcium channel blocker or monotherapy with disopyramide or ranolazine were excluded from the study. The primary composite functional endpoint was the proportion of patients who achieved either improvement of peak oxygen consumption (pVO_2) by at least 1.5 mL/kg/minute plus improvement in NYHA class by at least one or improvement of pVO_2 by at least 3 mL/kg/minute plus no worsening in NYHA class.

Secondary endpoints included treatment effects on LVOT obstruction, functional capacity, and health status; these were assessed by change from baseline through Week 30 in postexercise LVOT peak gradient, change in pVO_2, proportion of patients with improvement in NYHA class, a clinical summary questionnaire score, and a HCM symptom questionnaire shortness of breath domain score. At Week 30, 37% of the patients treated with mavacamten met the primary endpoint, compared with 17% of those receiving a placebo, and patients treated with mavacamten had greater improvement compared to the placebo group across all secondary endpoints.

Mavacamten reduces systolic contraction, and the most important concern with its use is the risk of heart failure due to systolic dysfunction; this is the topic of a boxed warning in its labeling and the basis for its restricted availability through the Camzyos REMS.

Patients who experience a serious intercurrent illness (e.g., serious infection) or arrhythmia (e.g., atrial fibrillation or other uncontrolled tachyarrhythmia) are at greater risk of heart failure. Echocardiogram assessments of LVEF are required prior to and during treatment with mavacamten. It is recommended that treatment not be initiated in patients with an LVEF of <55% and, that treatment be interrupted if LVEF is <50% at any visit, or if the patient experiences heart failure symptoms or worsening clinical status.

In the clinical trial, the mean absolute change from baseline in LVEF was –4% in those treated with mavacamten and 0% in those receiving a placebo. The boxed warning also identifies the increased risk of heart failure due to systolic dysfunction if mavacamten is used concurrently with certain cytochrome P450 inhibitors or if concurrent treatment with certain cytochrome P450 inducers is discontinued.

The adverse events most often

reported in the clinical study of mavacamten (and the incidence with the drug and placebo) include dizziness (27%, 18%) and syncope (6%, 2%). Treatment was discontinued in 0.8% of the patients treated with the new drug who experienced syncope.

There are no human data on the use of mavacamten during pregnancy but, based on results in animal studies, the drug is considered to have a risk of causing adverse developmental events. The absence of pregnancy should be confirmed before treatment is initiated, and females of reproductive potential should be advised to use effective contraception during treatment with mavacamten and for 4 months after the last dose. Because mavacamten may reduce the concentration and activity of estrogens and progestins included in hormonal contraceptive products, an alternative nonhormonal contraceptive method should be used or added. There is a pregnancy safety study for mavacamten and, if it is administered during pregnancy or if a patient becomes pregnant during treatment or within 4 months of the last dose, exposure should be reported to the company at 1-800-721-5072 or www.bms.com.

The estimated oral bioavailability of mavacamten is at least 85%, and it is extensively metabolized via the CYP2C19 (74%), CYP3A4 (18%), and CYP2C9 (8%) pathways. The half-life of the drug is significantly prolonged in patients who are poor CYP2C19 metabolizers, who are more prevalent in Asian populations. Approximately 85% of a dose is recovered in the urine, almost entirely in the form of metabolites, and dosage adjustment is not needed in patients with mild to moderate renal impairment. Although mavacamten exposure is markedly increased in patients with mild to moderate hepatic impairment, the initial dosage does not need to be adjusted and subsequent changes in dosage are addressed with the use of the recommended dose titration algorithm and monitoring plan. The effects of severe hepatic impairment and severe renal impairment on the activity of mavacamten are not known.

As a substrate for multiple metabolic pathways, mavacamten may interact with dozens of other medications, including certain nonprescription medications (e.g., omeprazole) and dietary supplements (e.g., St. John's wort).

Concurrent use with moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors is contraindicated because of the likelihood of increased activity of mavacamten and the risk of heart failure. Examples of these products include most azole antifungal drugs, clarithromycin, ritonavir, esomeprazole, omeprazole (40 mg once a day), and grapefruit.

Concurrent use of moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers is also contraindicated because of the probability of reduced activity of mavacamten and reduced efficacy. Examples of these products include carbamazepine, phenytoin, and St. John's wort.

The use of weak CYP2C19 inhibitors or moderate CYP3A4 inhibitors may increase the activity of mavacamten, but to a lesser extent than what occurs with strong inhibitors, and the dosage of the new agent should be reduced when used concurrently. Examples of these products include diltiazem, verapamil, cimetidine, and omeprazole (20 mg once a day).

A longer (but also incomplete) list of these groups of medications is provided in the Drug Interaction and Counseling Checklist for Pharmacies in the Camzyos REMS document available at camzyosrems.com. The interaction with omeprazole provided in this information is of particular interest because concurrent use of the higher dosage of 40 mg once a day with mavacamten is contraindicated, whereas the dosage of 20 mg once a day may be used concurrently with mavacamten in a lower dosage.

The concurrent use of mavacamten with other drugs that reduce cardiac contractility may result in negative inotropic effects. Most of the patients in the clinical trial of mavacamten were also treated with a beta blocker, diltiazem, or verapamil, and the latter two agents are among those that inhibit cytochrome P450 metabolic pathway(s) to an extent that a reduction in dosage of mavacamten is recommended. The use of mavacamten should be avoided in patients taking disopyramide, ranolazine, verapamil with a beta blocker, or diltiazem with a beta blocker, as these medications and combinations increase the risk of left ventricular systolic dysfunction and heart failure symptoms and clinical experience is limited. If concomitant therapy with a negative inotrope is initiated, or if the dose of a negative inotrope is increased, LVEF should be closely monitored until stable doses and clinical response have been achieved.

Mavacamten is an inducer of CYP3A4, CYP2C19, and CYP2C9 and concurrent use with substrates of these pathways such as hormonal contraceptives and omeprazole may reduce the activity of the latter agents.

Daily dosing with mavacamten takes weeks to achieve steady-state drug concentrations and therapeutic effects, and genetic variation in metabolism and drug interactions may cause large differences in exposure. Initiation of treatment or up-titration of dosage of the drug is not recommended in patients with LVEF of <55%.

When initiating or titrating mavacamten, the LVEF should first be considered, and then the Valsalva LVOT gradient and patient's clinical status. The Valsalva maneuver is used to stim-

Comparison of mavacamten with beta blockers (e.g., metoprolol)

Advantages

- It is more effective than previous treatments and may reduce the need for surgery.
- It has a unique mechanism of action (i.e., as a cardiac myosin inhibitor) and is the first drug to target the underlying pathology of the disease.

Disadvantages

- It may cause serious adverse events (e.g., heart failure) and interact with many other medications.
- Monitoring treatment is more complex.
- It may cause adverse developmental effects if used during pregnancy.

ulate a response that provides added understanding and interpretation of electrocardiography procedures. The recommended starting dosage is 5 mg orally once a day without regard to food, and the maximum recommended dosage is 15 mg once a day. The product labeling should be consulted for the algorithms for initiation and maintenance for appropriate dosing and monitoring schedules for the new agent. Treatment should be evaluated every 4 weeks for the first 12 weeks and every 12 weeks after a stable maintenance dosage has been established. If the LVEF falls below 50%, treatment should be interrupted, and the algorithm should be consulted for guidance on restarting or discontinuing treatment. Treatment should be permanently discontinued in patients taking a dose of 2.5 mg once a day who experience a reduction in LVEF to <50% on two occasions.

Mavacamten capsules are supplied in 2.5 mg, 5 mg, 10 mg, and 15 mg potencies.

Antiasthmatic agent

The symptoms of asthma can be effectively managed in many patients with maintenance treatment with a long-acting beta$_2$-adrenergic agonist (LABA), long-acting muscarinic antagonist, and/or an inhaled corticosteroid via oral inhalation. Many combination formulations of these agents are available, including several (e.g., Trelegy Ellipta) that contain agents in all three of these classes of medications (vilanterol, umeclidinium, fluticasone). Certain corticosteroids (e.g., prednisone) are sometimes administered orally in patients with more severe symptoms. Even though these regimens are effective in most patients with asthma, some patients do not experience adequate reduction of symptoms and associated complications with conventional therapy, and there continue to be numerous asthma-related hospitalizations.

Multiple cell types, including eosinophils and mediators (e.g., cytokines) are involved in the inflammatory process that occurs in the airways of the lungs in patients with asthma. Interleukin-5 (IL-5) is a major cytokine responsible for growth and differentiation, recruitment, activation, and survival of eosinophils.

In 2015, mepolizumab (Nucala—GlaxoSmithKline) was approved as the first IL-5 antagonist for add-on maintenance treatment of patients with severe asthma and an eosinophilic phenotype. Reslizumab (Cinqair—Teva Respiratory, LLC) and benralizumab (Fasenra—AstraZeneca AB) are also IL-5 antagonists that have since been approved for the same indication, and mepolizumab has been approved for additional indications.

Dupilumab (Dupixent—Regeneron Pharmaceuticals) is an IL-4 antagonist that was initially approved in 2017 for the treatment of patients with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when these therapies are not advisable. It has subsequently been approved for several additional indications, including as add-on maintenance treatment of patients with moderate to severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma. All four of these drugs are monoclonal antibodies that are administered subcutaneously.

Thymic stromal lymphopoietin (TSLP) is a cytokine mainly derived from epithelial cells and occupies an upstream position in the asthma inflammatory cascade.

Tezepelumab-ekko is the newest monoclonal antibody to be indicated for the treatment of patients with severe asthma and, like the biologics identified above, is administered subcutaneously.

It is the first TSLP blocker to be approved and reduces cytokines and biomarkers associated with inflammation including blood eosinophils, airway submucosal eosinophils, IL-5, IL-13, and other mediators of inflammation. It is specifically indicated for the add-on maintenance treatment of adult and pediatric patients ages 12 years and older with severe asthma.

It has an important advantage over previous agents in that its indication is not limited by a need to identify a phenotype or biomarker.

The effectiveness of tezepelumab was demonstrated in two placebo-controlled, 52-week studies in which the primary endpoint was the rate of clinically significant asthma exacerbations, defined as worsening of asthma requiring the use of or increase in oral or injectable corticosteroids for at least 3 days, a single depo-injection of corticosteroids, and/or emergency department visits requiring use of oral or injectable corticosteroids and/or hospitalization. Patients treated with tezepelumab experienced significant reductions compared to placebo in the annualized asthma exacerbation rate (0.93 compared with 2.1, respectively, in the largest study), and fewer exacerbations requiring emergency department visits/hospitalizations (0.06, 0.28), and exacerbations requiring hospitalizations (0.03, 0.19). The change from baseline in forced expiratory volume in 1 second (FEV_1) was assessed as a secondary endpoint, and patients treated with tezepelumab experienced consistent improvements in the increase in FEV_1. In another study in which patients with severe asthma were being treated with oral corticosteroids, the use of tezepelumab did not provide a statistically significant reduction in the maintenance dosage of the corticosteroid.

The monoclonal antibodies used for treating patients with severe asthma should not be used for the relief of acute bronchospasm or status asthmaticus. Both mepolizumab and dupilumab have been approved for additional indications (e.g., chronic rhinosinusitis with nasal polyps), but these are not labeled indications for tezepelumab at present.

Tezepelumab was well-tolerated in the clinical studies, with the most commonly reported adverse events including pharyngitis (4%), arthralgia (4%), back pain (4%), and injection site reaction (3%). Hypersensitivity reactions have also occurred.

If the use of tezepelumab permits a reduction in dosage of a corticosteroid that has been part of a patient's maintenance treatment, the dosage should be reduced gradually to reduce the risk of systemic withdrawal symptoms and/or unmasking of conditions

Comparison of tezepelumab with IL-5 antagonists (mepolizumab is used for comparisons)

Advantages

- Its use is not limited to patients with an eosinophilic phenotype.
- It has a unique mechanism of action (i.e., TSLP blocker).

Disadvantages

- Labeled indications are more limited (whereas mepolizumab also has labeled indications for chronic rhinosinusitis with nasal polyps, eosinophilic granulomatosis with polyangiitis, and hypereosinophilic syndrome).
- Safety in patients less than 12 years old has not been established (whereas mepolizumab is indicated for use in patients 6 years and older).
- It has not been directly compared with previous agents in clinical studies.

previously suppressed by systemic corticosteroid therapy.

Because eosinophils may be involved in the immunological response to helminth infections, patients with these infections were excluded from the clinical trials. It is not known if tezepelumab will influence a patient's response to helminth infections, so a pre-existing helminth infection should be treated before initiating therapy with the new drug. If a helminth infection occurs during treatment with tezepelumab and does not respond to antihelminth treatment, tezepelimab should be discontinued until the infection resolves.

The use of live attenuated vaccines in patients treated with tezepelumab has not been evaluated, and the use of these vaccines during treatment should be avoided.

Information on the use of tezepelumab during pregnancy is very limited, but the use of high doses in animal studies has not identified concerns. The effectiveness and safety of the new drug in patients younger than 12 years old have not been evaluated.

Following subcutaneous administration, the estimated absolute bioavailability of tezepelumab is approximately 77%. The drug is degraded by proteolytic enzymes and not metabolized by hepatic enzymes. Changes in hepatic or renal function are not expected to influence clearance.

Tezepelumab is injected subcutaneously into the upper arm, thigh, or abdomen, and the recommended dosage is 210 mg every 4 weeks. The IL-5 antagonist benralizumab is administered every 8 weeks during maintenance treatment, whereas mepolizumab is administered every 4 weeks. Tezepelumab injection is supplied in single-dose glass vials, single-dose prefilled syringes, and single-dose prefilled pens containing 210 mg/1.91 mL. The vial and prefilled syringe are intended for administration by a health care provider, whereas the prefilled pen can be administered by patients, caregivers, or health care providers. The products should be stored in a refrigerator in the original carton to protect from light until the time of use. Following removal from the refrigerator, the drug must be used within 30 days or discarded.

Antifungal agent

Vulvovaginal candidiasis (VVC) is one of the most common vaginal infections and is usually caused by *Candida albicans*, although other species of *Candida* may be the causative agent in some patients. A single oral dose of fluconazole or the intravaginal administration of an azole antifungal agent has been highly effective in the treatment of these infections.

However, increasing resistance to the azole antifungal agents has occurred, and approximately 10% of patients have experienced recurrent VVC (RVVC), defined as three or more episodes of symptomatic VVC in less than 1 year. RVVC may be treated with the same azole antifungal used for initial treatment and/or with a suppressive maintenance regimen with oral fluconazole. Other antifungal agents such as ibrexafungerp (Brexafemme—Scynexis) may also be considered for treatment.

Oteseconazole is an orally administered azole antifungal agent with a long duration of action. Ergosterol is required for fungal cell membrane formation and integrity, and oteseconazole inhibits 14-alpha-demethylase, an enzyme that catalyzes an early step in the biosynthetic pathway of ergosterol. In vitro study results suggest that it may be active against certain species of *Candida* that are resistant to fluconazole.

Oteseconazole is indicated to reduce the incidence of RVVC in females with a history of RVVC who are not of reproductive potential. It is the first drug to be approved in the U.S. for RVVC, although ibrexafungerp was approved for the additional indication of RVVC in late 2022 following its initial approval in 2021 for the treatment of VVC.

Oteseconazole was evaluated in two placebo-controlled clinical trials that included an induction phase and maintenance phase. Patients received

Accreditation information
Provider: APhA
Target audience: Pharmacists
Release date: August 1, 2023
Expiration date: August 1, 2026
Learning level: 2
ACPE Universal Activity Number: 202-0000-23-314-H01-P
CPE credit: 1 hour (0.1 CEU)
Fee: There is no fee associated with this activity for APhA members. There is a $25 fee for nonmembers.

APhA is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education (CPE). The ACPE Universal Activity Number assigned to this activity by the accredited provider is 0202-0000-23-314-H01-P.

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Development: This home-study CPE activity was developed by APhA.

three sequential doses of 150 mg of fluconazole (every 72 hours) on Days 1, 4, and 7 during the induction phase, then returned 14 days after the first dose of fluconazole. If the acute VVC was resolved, they were randomized to receive either 150 mg of oteseconazole or placebo daily for 7 days, followed by 11 weekly doses in the maintenance phase. Efficacy was assessed by the proportion of patients with one or more culture-verified acute VVC episodes during the maintenance phase through Week 48. In the two studies, 6.7% and 3.9% of the patients treated with the new drug experienced an acute VVC episode, compared with 42.8% and 39.4%, respectively, of those receiving placebo.

The efficacy of oteseconazole and fluconazole plus placebo was compared in a third clinical trial in which patients were treated with either oteseconazole or fluconazole during the induction phase. Patients returned 14 days after the first dose and moved to the maintenance phase if the acute VVC episode was resolved. During the maintenance phase, patients treated with oteseconazole during the induction phase received 150 mg oteseconazole once a week for 11 weeks, and those treated with fluconazole during the induction phase received placebo once a week for 11 weeks. Patients were evaluated through Week 50 and oteseconazole was superior to fluconazole/placebo with acute VVC episodes reported in 10.3% and 42.9% of patients, respectively.

Headache (7%) and nausea (4%) are the most frequently reported adverse events with the use of oteseconazole.

The most important concern with its use is the risk of adverse developmental events (e.g., ocular abnormalities) if it is used during pregnancy, based on results of studies in animals. The labeled indication is more restrictive than those for other antifungal agents used for VVC, and limits use to females who are not of reproductive potential, defined as patients who are postmenopausal or have another reason for permanent infertility (e.g., tubal ligation, hysterectomy). Oteseconazole is contraindicated in females of reproductive potential, including those using contraception, and in pregnant and lactating women. The drug has a half-life of approximately 140 days, and the long period of exposure and persistence in the tissues precludes adequate mitigation of developmental toxicity risks.

Oteseconazole is administered orally with food. It does not undergo significant metabolism and, unlike most other antifungal azoles, is not likely to interact with other drugs that inhibit or induce cytochrome P450 metabolic pathways. Approximately 56% of a dose is recovered in the feces and 26% in the urine. Because there are insufficient data to assess its safety, the use of oteseconazole is not recommended in patients with moderate or severe hepatic impairment or severe renal impairment.

The new drug inhibits the breast cancer resistance protein (BCRP) and may increase the exposure and risk of adverse events of BCRP substrates (e.g., rosuvastatin). If used concurrently, the lowest possible starting dose of the BCRP substrate should be used or a reduction in dosage of the BCRP substrate considered.

Oteseconazole capsules are supplied in a 150 mg potency in 18-count blister packages. Capsules should be administered with food and swallowed whole. There are two dosage regimens: One in which oteseconazole is used as a single agent and the other in which it is used in conjunction with fluconazole. When used alone, a dose of 600 mg (4 capsules) is administered on Day 1; a dose of 450 mg (3 capsules) on Day 2; and beginning on Day 14, a dosage of 150 mg once a week (every 7 days) for 11 weeks. In the regimen in which it is used with fluconazole, a dose of 150 mg of fluconazole is administered on Days 1, 4, and 7, and oteseconazole is administered in a dosage of 150 mg once a day for 7 days on Days 14–20, and then beginning 150 mg once a week (every 7 days) on Day 28 for 11 weeks.

Fluconazole is not supplied in the carton with the blister package containing oteseconazole. ■

Comparison of oteseconazole with fluconazole

Advantages

- It may be more effective, and its activity may include species of Candida that are resistant to fluconazole.
- It is the first drug to be approved with a labeled indication for RVVC.
- It is less likely to interact with other medications.

Disadvantages

- It is more likely to cause adverse developmental effects if used during pregnancy and use is contraindicated.
- Labeling is more restrictive in limiting use to females with a history of RVVC who are not of reproductive potential.

CPE information

To obtain 1 hour of CPE credit for this activity, complete the CPE exam and submit it online at www.pharmacist.com/education. A Statement of Credit will be awarded for a passing grade of 70% or better. You have two opportunities to successfully complete the CPE exam. Pharmacists and technicians who successfully complete this activity before October 1, 2025, can receive credit. Your Statement of Credit will be available online immediately upon successful completion of the CPE exam.

This policy is intended to maintain the integrity of the CPE activity. Learners who successfully complete this activity by the expiration date can receive CPE credit. Please visit CPE Monitor for your statement of credit/transcript.

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Assistance is available Monday through Friday from 8:30 am to 5:00 pm ET at APhA InfoCenter by calling 800-237-APhA (2742) or by e-mailing infocenter@aphanet.org.

CPE Assessment

This assessment must be taken online; please see "CPE information" in the sidebar on the previous page for further instructions. The online system will present these questions in random order to help reinforce the learning opportunity. There is only one correct answer to each question.

1. **Which of the following agents acts as a thymic stromal lymphoprotein blocker?**
   a. Inclisiran
   b. Mavacamten
   c. Tezepelumab
   d. Oteseconazole

2. **Which of the following agents is used to reduce low-density lipoprotein cholesterol (LDL-C) concentrations?**
   a. Inclisiran
   b. Mavacamten
   c. Tezepelumab
   d. Oteseconazole

3. **Which of the following agents is administered once a day?**
   a. Inclisiran
   b. Mavacamten
   c. Tezepelumab
   d. Oteseconazole

4. **Which of the following agents is contraindicated in females of reproductive potential, including those who are using contraception?**
   a. Inclisiran
   b. Mavacamten
   c. Tezepelumab
   d. Oteseconazole

5. **Which of the following statements is correct regarding inclisiran?**
   a. It has been demonstrated to reduce the risk of adverse CV events.
   b. It is administered intramuscularly.
   c. It is administered once every 6 months during maintenance treatment.
   d. Concurrent use with a moderate or strong CYP3A4 inhibitor is contraindicated.

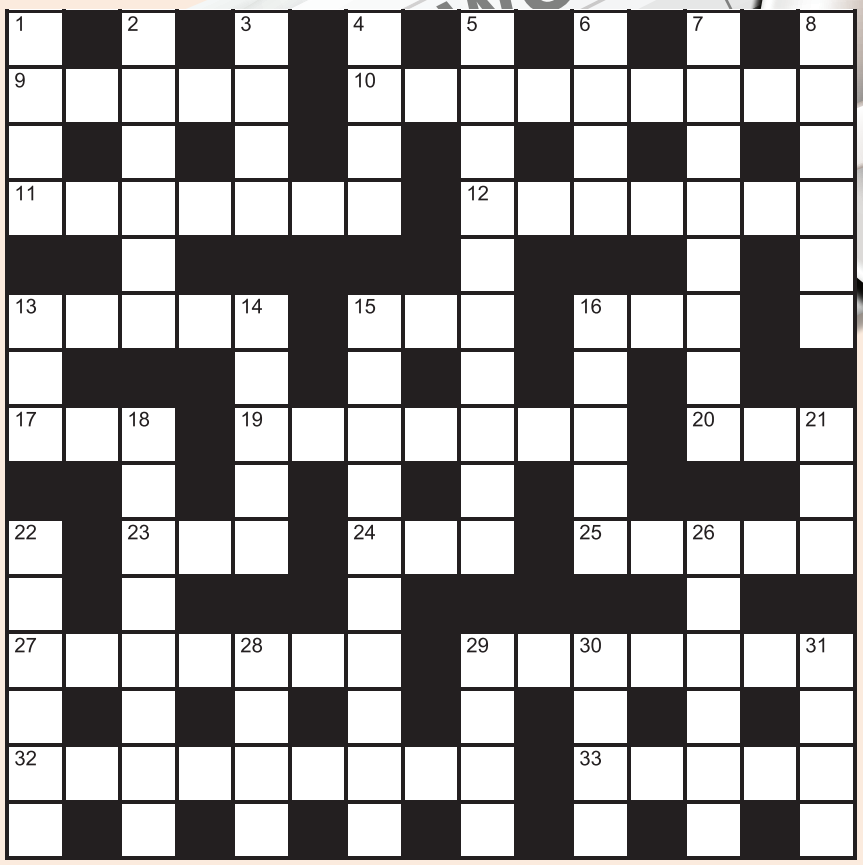
6. **Which of the following statements is correct regarding mavacamten?**
   a. It is used to increase left ventricular ejection fraction (LVEF) in patients in whom LVEF is <50%.
   b. It is used in a combination regimen with disopyramide, metoprolol, and amlodipine.
   c. It is not metabolized and is eliminated in unchanged form in the urine.
   d. It may reduce the activity of estrogens and progestins and an alternative nonhormonal contraceptive method should be used or added.

7. **Which of the following statements is correct regarding tezepelumab?**
   a. Its use should be limited to patients with severe asthma who have an eosinophilic phenotype.
   b. It is administered once every 4 weeks.
   c. Bradycardia is the adverse event most often associated with its use.
   d. Concurrent use with a strong CYP2C19 inhibitor is contraindicated.

8. **Which of the following statements is correct regarding oteseconazole?**
   a. It may increase the activity of rosuvastatin.
   b. It is a prodrug that is converted to clotrimazole following administration.
   c. It should be administered apart from food.
   d. It should be administered once a day for a period of 11 weeks.

9. **Which of the following statements is correct regarding the comparison of oteseconazole and fluconazole?**
   a. Oteseconazole is more likely to interact with other medications.
   b. The activity of oteseconazole may include species of *Candida* that are resistant to fluconazole.
   c. Oteseconazole is considered safer for use during pregnancy.
   d. Oteseconazole has a short duration of action and must be administered concurrently with fluconazole.

10. **Which of the following statements is correct regarding the comparison of inclisiran and evolocumab?**
    a. The indications for both agents are for use as an adjunct to diet and maximally tolerated statin therapy.
    b. Evolocumab has a longer duration of action and is administered less frequently than inclisiran.
    c. Inclisiran is an HMG-CoA reductase inhibitor, and evolocumab is a PCSK9 inhibitor.
    d. Inclisiran reduces the synthesis of PCSK9, and evolocumab is an inhibitor of PCSK9.



Across

9 Some patients are allergic to this antibiotic component
10 Type of exercise that builds strength
11 Muscular weakness or partial paralysis
12 The time you seem to be on hold with insurance companies
13 Administered medicine
15 Medication approval org.
16 Psychedelic often studied for its effects
17 The messenger form of this stimulates immune response with the COVID-19 vaccine
19 Air carrier?
20 Virus that can cause respiratory illness
23 Tyrannosaurus ___
24 Withdrawal symptom, in short
25 Facial cavity often the target of pseudoephedrine
27 Inconsequential
32 Sleep supplement
33 Emotionally demanding

Down

1 Org. devoted to medication safety
2 These often pop up with drug–drug interactions
3 Cause of a 2002 viral outbreak
4 PREP target
5 Unpleasant menopause symptoms
6 Treatments for dry eyes may cause one of these
7 Status earned by pharmacists
8 Disease caused by a vitamin C deficiency
13 Fees taken by payers after a Medicare prescription is filled
14 When patients have 24-across they may need this
15 Pharmacists are always alert for this type of prescription
16 Slow drips
18 With skill
21 ___ deferens
22 Disease that usually requires inhalers
26 Common adverse effect of many medications
28 Bit
29 0.473 liters
30 Topical salicylic acid can be used to treat this skin condition
31 Eye affliction that may require antibiotic treatment

Solution is available online at pharmacytoday.org.