PharmacyToday

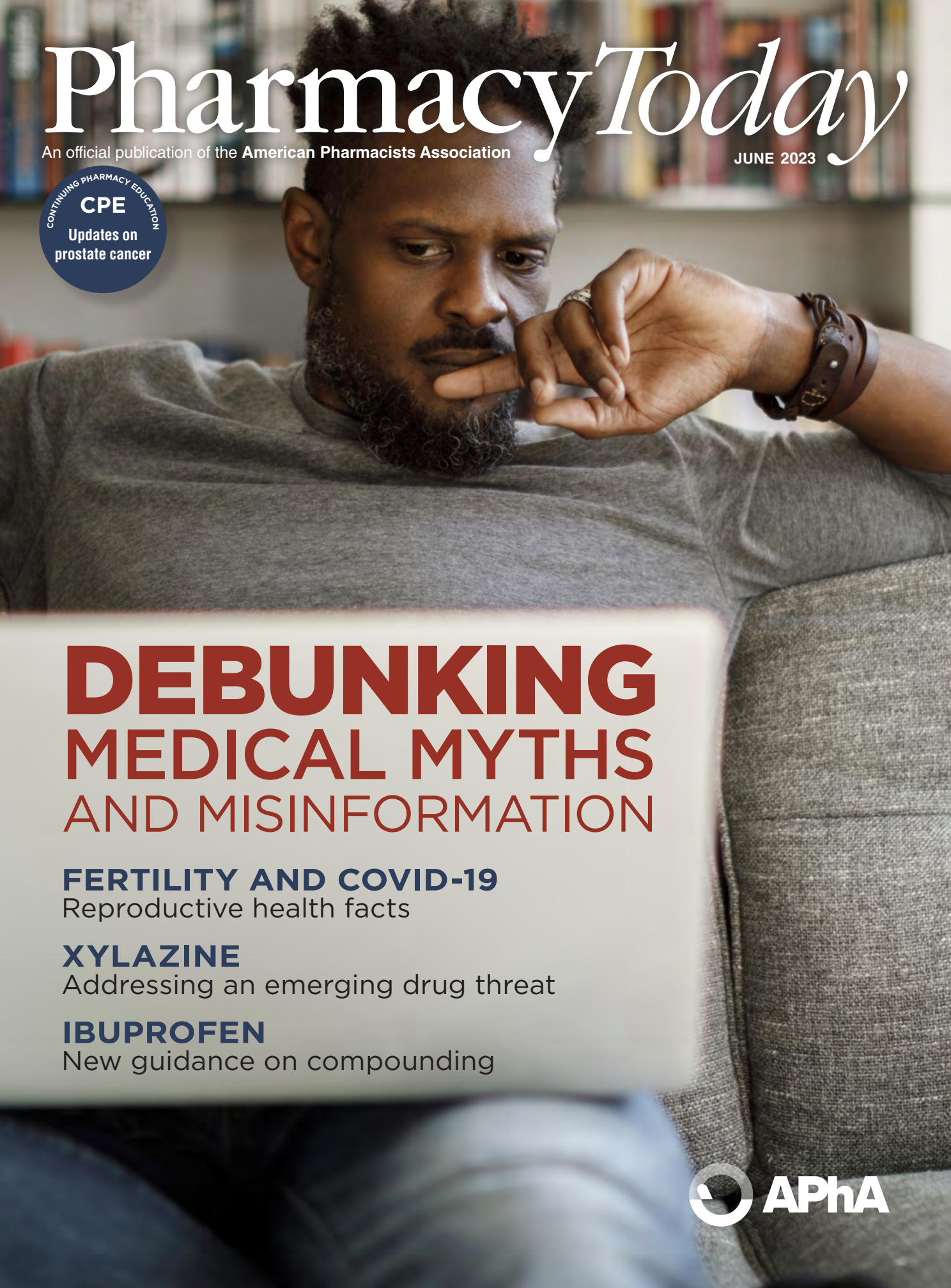
An official publication of the **American Pharmacists Association**

JUNE 2023

CONTINUING PHARMACY EDUCATION

CPE

Updates on prostate cancer



DEBUNKING MEDICAL MYTHS AND MISINFORMATION

FERTILITY AND COVID-19
Reproductive health facts

XYLAZINE
Addressing an emerging drug threat

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New guidance on compounding

APhA

BulletinToday

Need for more patient–provider dialogue as deprescribing medicine for older adults catches on

Findings from the University of Michigan National Poll on Healthy Aging suggest that older adults are supportive of the idea of deprescribing medications.

The survey found that 82% of adults ages 50 to 80 years old would be willing to stop taking one or more of the prescription medicines they have been using for more than a year if a health care provider said it was feasible.

The survey also revealed that 26% of respondents have already done so in the past 2 years.

"Deprescribing, which can include prescription medications, over-the-counter medications, and dietary supplements, should be based on dialogue between patients and providers, and sometimes family members," said Sarah Vordenberg, PharmD, MPH, a University of Michigan College of Pharmacy clinical associate professor who worked on the poll, in a statement.

More than a third of the older adults who said they stopped taking a prescription medication that they had been using for more than a year said they did so without consulting a health professional. The poll also found that 82% of people 50 to 80 years old take at least one prescription medicine regularly; of those 28% said they believe they take too many medications.

More than one-half of respondents said they take three or more prescription medications; 11% said they take three or more OTC medicines regularly; and 38% take three or more vitamins, minerals, or supplements.

The survey also indicated that more people should use a comprehensive medication review by a pharmacist or other provider—a benefit offered by Medicare and other insurance.

"While we found that over 90% of older adults who take at least one prescription medicine expect their provider to review their list of medicines at least annually, research has shown this is often not the case," Vordenberg said. ■

FDA approves RSV vaccine for older adults

FDA approved GSK's respiratory syncytial virus (RSV) vaccine (Arexvy) for adults aged 60 years and older.

GSK anticipates the vaccine will be available in pharmacies, clinics, and other health care sites this fall. GSK has not yet released a price, but insurance companies usually pay for much of the cost of many vaccines.

A recent study published in *NEJM* found that GSK's vaccine was nearly 83% effective in preventing lower respiratory tract illness in adults ages 60 years and older.

In March 2023, an FDA advisory panel reviewed data from trials for two RSV vaccines designed for older adults: one developed by GSK and another by Pfizer. The panel advised FDA to approve both vaccines.

According to data provided to the FDA panel, two individuals in the trial who received the Pfizer vaccine and one individual who received the GSK vaccine developed Guillain-Barré syndrome 2 days after the vaccines were administered.

RSV causes roughly 6,000 to 10,000 deaths annually in adults ages 65 years and older and at least 60,000 annual hospitalizations in that age group. It is also a leading cause of death among children globally. ■

Most children recover from Lyme disease within 6 months of treatment, says study

New findings from researchers at the National Institute of Allergy and Infectious Disease (NIAID) conclude that most children with Lyme disease recovered from their symptoms within 6 months.

The findings, which were based on survey responses from the parents of 102 children ages 5 to 18 years, revealed that 75% of children fully recovered within 6 months of completing antibiotic treatment: 31% of all children recovered within 1 month; 30% recovered in 1 to 3 months; and 14% recovered in 4 to 6 months.

Approximately 22% of children in the study experienced at least one symptom that persisted 6 or more months after completing treatment. Of those, 9% had symptoms classified as post-treatment Lyme disease (PTLD) syndrome. Six percent of the children were not fully recovered at the time of the survey, with 1% experiencing symptoms significant enough to impair daily functioning, the authors noted.

The children had all been diagnosed with Lyme disease between 6 months and 10 years before enrollment. Adolescents ages 10 to 18 years old were also invited to complete adolescent-specific questionnaires.

Antibiotic treatment resulting in full recovery is successful in most Lyme cases.

Common symptoms of Lyme disease include fever, headache, fatigue, and a distinct skin rash called erythema migrans. Without treatment, the infection can spread to joints, the heart, and the nervous system.

For some, however, symptoms of pain, fatigue, or difficulty thinking persist or return after antibiotic treatment. Symptoms that substantially reduce levels of activity and impact quality of life for more than 6 months after treatment are classified as PTLD syndrome.

According to the researchers, who were from NIAID and the Children's National Research Institute, the study supports previous data showing an excellent overall prognosis for children with Lyme disease, which should help alleviate understandable parental and guardian stress associated with lingering nonspecific symptoms among infected children.

The research team also suggested these new data could help reduce the potential for families seeking dangerous alternative therapies for children who experience prolonged recovery times. PTLD syndrome remains poorly understood in children and adults, and more research is needed to better recognize these prolonged symptoms and identify treatment targets, according to the authors. ■

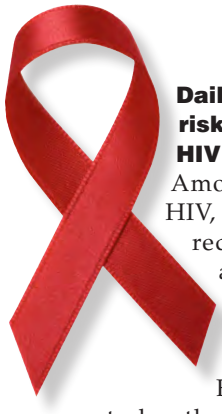
DEA announces extension for telemedicine prescribing of certain drugs

DEA has said that for now it is extending emergency telehealth policies set during the COVID-19 pandemic, enabling certain health care providers to have greater leeway in prescribing some controlled substances.

The DEA decision affects buprenorphine for opioid addiction and stimulants such as amphetamine/dextroamphetamine (Adderall—Teva Pharmaceutics) used to treat ADHD.

"We recognize the importance of telemedicine in providing Americans with access to needed medications, and we have decided to extend the current flexibilities while we work to find a way forward to give Americans that access with appropriate safeguards," said DEA administrator Anne Milgram.

Because of DEA's extension of the policies, health care providers may write buprenorphine prescriptions to patients after evaluating them via phone or video. DEA also introduced new policies for buprenorphine that would require patients to visit their prescriber for an in-person exam within 30 days, and patients who began buprenorphine treatment under emergency rules would have a 180-day grace period before they would need to visit their provider in person. ■



Daily statin reduces CVD risk for those living with HIV

Among people living with HIV, a daily statin medication reduced the risk of CVD, according to results from a large NIH study.

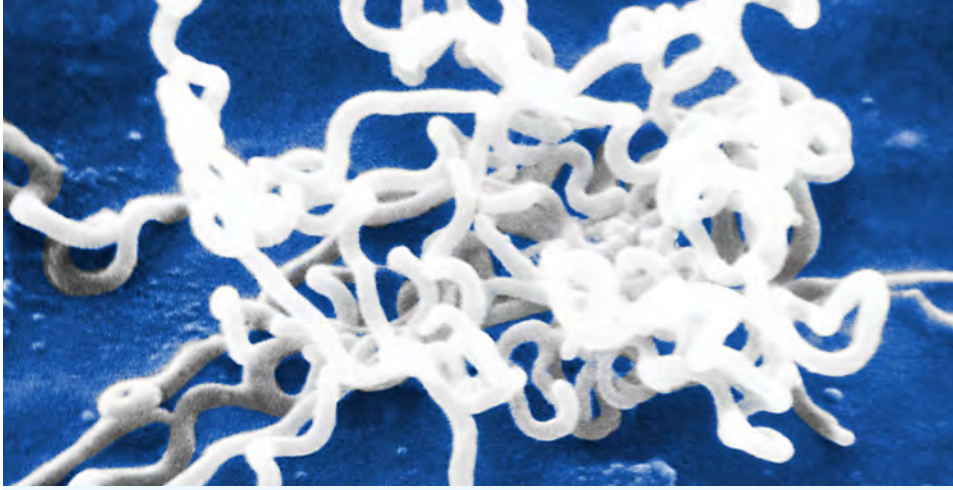
The Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study—the first large-scale clinical trial to test a primary cardiovascular prevention strategy in this population—found that participants who took pitavastatin calcium (a daily statin) lowered their risk of major adverse cardiovascular events by 35% compared to those taking a placebo. The trial was stopped early because of adequate evidence for efficacy.

Adverse drug events observed in the study were like those for the general population taking statin therapy.

"The REPRIEVE study reflects the evolution of HIV science, and progress from focusing mostly on approaches to treat and control the virus to finding ways to improve the overall health of people living with HIV," said Hugh Auchincloss, MD, acting director for the National Institute of Allergy and Infectious Diseases, in a press statement.

Decades of research and advances in HIV treatment have drastically reduced AIDS-related complications and deaths. As people with HIV live longer, premature heart disease and other chronic conditions have emerged as leading causes of morbidity and mortality, contributing to persistent gaps in lifespan between people with HIV and the broader population.

In 2015, a total of 7,769 volunteers entered the clinical trial. Participants were 40 to 75 years old and more than 30% were women. They were all taking antiretroviral therapy, with CD4+ cell counts greater than 100 cells/mm^3 and had low-to-moderate traditional CVD risk that would not typically be considered for statin treatment. The trial was conducted in 12 countries in Asia, Europe, North America, South America, and Africa. ■



CDC finds alarming trends in STIs, especially rise in syphilis cases

A new CDC report found that recorded cases of sexually transmitted infections (STIs) in U.S. patients continued to increase between 2020 and 2021.

While gonorrhea rates increased more than 4%, syphilis rates jumped by nearly 32% for all stages of the infection, with a total of 176,713 syphilis cases recorded in 2021. The last time cases were nearly this high was in 1950, when 217,558 cases were reported.

The report also found that cases of congenital syphilis, which happens when a baby is born with the infection after the mother passed it on during pregnancy, rose by 32%—from 2,148 to more than 2,800—with 220 stillbirths and infant deaths as a result.

Chlamydia rates increased nearly 4%, but—unlike gonorrhea and syphilis—still did not return to pre-pandemic levels. CDC said this raises concerns that screening continued to be affected by disruptions from COVID-19 during the second year of the pandemic.

CDC noted that while STIs are common in all groups and regions nationwide, some communities are particularly affected, such as bisexual and gay men and younger people. A disproportionate number of cases were diagnosed among American Indian/Alaska Native and Black/African American communities.

The report calls for expanded efforts with ubiquitous STI testing and treatment programs and in developing and approving more point-of-care rapid tests and self-tests as well as taking steps to advance scientific research in areas such as vaccines and post-exposure prophylaxis.

"For the first time in decades, we're seeing promising new STI interventions on the horizon, but these alone will not solve this epidemic. It will take many of us working together to effectively use new and existing tools, to increase access to quality sexual health care services for more people, and to encourage ongoing innovation and prioritization of STI prevention and treatment in this country," said Leandro Mena, MD, MPH, director of CDC's division of STD prevention, in a CDC news release. ■

Study finds COVID-19 may increase risk of type 2 diabetes

Researchers recently reported that individuals infected with COVID-19 were significantly more likely to be diagnosed with type 2 diabetes within 1 year of their infection compared with those who had not been exposed to the virus. They also found that men were more likely than women to develop diabetes.

Additionally, those admitted to intensive care with COVID-19 were more than three times as likely to develop diabetes, according to the study findings.

The study, published on April 18, 2023, in *JAMA Network Open*, used a large data set from British Columbia to compare diabetes diagnoses among more than 125,000 individuals who had tested positive for COVID-19 in 2020 and 2021 with those of more than 500,000 unexposed individuals during the same period.

More than a dozen studies have examined the link between COVID-19 and diabetes, and a majority have reported an increase in diagnosis following infection as well as higher risks for men and those with severe disease. ■

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Take the Crossword Challenge

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Combating medical myths: Pharmacists are essential

Patients often take action on their health and wellness based on what they hear on TV. Surprising, but true. According to CDC, over a 6-month period, nearly three-quarters of primetime viewers in the United States reported learning something new about a health or wellness topic simply by watching TV.

Although there are reputable sources of health information on TV, social media channels, in the news media, or via messaging apps, these can also be sources of misinformation for patients.

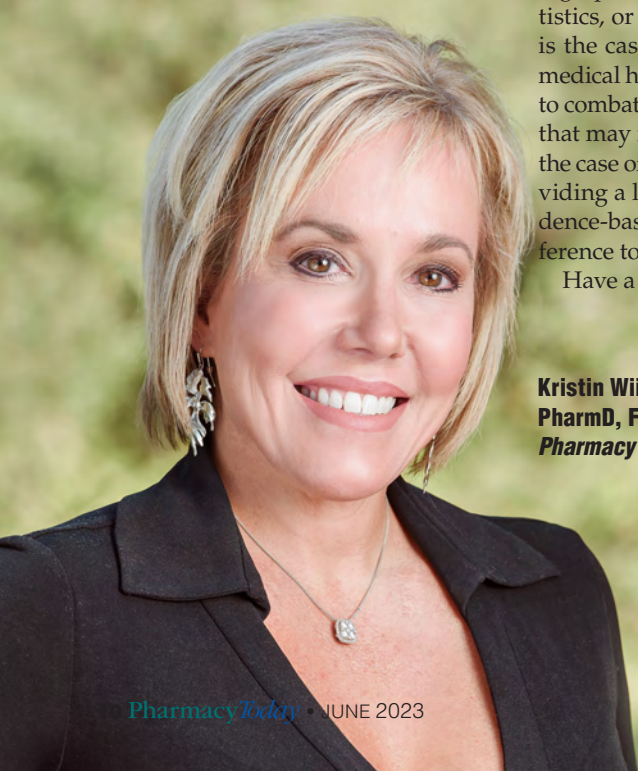
This month's *Pharmacy Today* cover story delves into the harmful impact of medical misinformation—and disinformation (i.e., intentional dissemination of falsehoods)—and what pharmacists can do to help. According to the story, medical misinformation can lead to vaccine hesitancy, medication noncompliance, disease outbreaks, hospitalization, and even death.

Pharmacists play a key role in helping to debunk medical falsehoods. Proactively educating patients from the start, before they encounter false information, is particularly effective. It's harder to undo a belief than it is to prevent it. By listening to patients, asking open-ended questions in a nonjudgmental manner, and referring patients to credible sources, pharmacists can help prevent medical misinformation and patient harm.

In this issue of *Today*, you'll also find the latest on newly approved drugs including a new migraine-relief option, tips on counseling patients about sunscreens and sunburns, and get an update about helping patients with Alzheimer disease. Learn about the newest overdose threat in street opioids, how to help prevent childhood poisoning from opioids, and find an update on what you need to know about prostate cancer treatment in this month's CPE article.

Patients rely on their pharmacists to be sources of credible, unbiased scientific data about health, wellness, and medications. According to the University of California at San Francisco, combating medical misinformation also requires educating patients about potential red flags, including uncited or unsourced facts, information tied to selling a product, out-of-date studies or statistics, or claims of "miracle" cures. As is the case for other potential paths to medical harm, pharmacists are essential to combating negative patient outcomes that may result from medical myths. In the case of medical misinformation, providing a listening ear and targeted evidence-based education can make a difference to your patient's health.

Have a great *Today*! ■



Kristin Wiisanen
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***Pharmacy Today* editor in chief**

If you build it, they will come: A safe haven at the pharmacy

In the 1989 film *Field of Dreams,* an Iowa farmer is inspired to pursue a dream. He builds a baseball field on his farm driven by the promise that "if you build it, they will come." His pursuit of his dreams bring him amazing results: baseball fans came in droves to his small farm in Iowa.

Much like the main character, Ray Kinsella, so too are pharmacists working in dogged pursuit of new vistas, with the goal to continue to provide essential care to our nation's most vulnerable. During the pandemic, pharmacies and pharmacists built the field of availability and access for patient care services, and patients came in droves for immunizations, testing, and treatments.

The work of pharmacists has been nothing short of heroic. A new report from the IQVIA Institute for Human Data Science found that pharmacists in the United States administered more recommended routine vaccinations than physicians from 2020 to 2021. The report also finds that the majority of adult COVID-19 and shingles vaccinations took place at pharmacies as well as approximately 60% of vaccinations during flu season. The IQVIA data reveals a 30–40% increase in claims for flu vaccines at pharmacies between 2018 and 2019 as well as in 2020. The report also shows that pneumococcal vaccinations increased at pharmacies, and roughly 13–20% of adult HPV vaccines were administered at a pharmacy by the end of 2021 compared with 5–8% in 2018.

The PREP Act gave pharmacists the temporary ability to vaccinate patients as young as 3 years old, thus helping to fulfill the increasing demand for vaccinations that followed the rise of COVID-19 and close the gaps in access for low-income families and rural communities. The IQVIA report found that there were 15% more pharmacy locations within low-income communities than physician's offices, meaning that lower-income people had more access to pharmacists than to physicians and could count on their pharmacist for timely care.

Although the PREP Act authorities have been extended, access for these patient care services at pharmacies is temporary for seniors because pharmacists are not considered providers under Medicare. Congress has recognized this gap with the introduction of federal legislation, H.R. 1770, the Equitable Community Access to Pharmacists Services Act. And just last month, Senators Chuck Grassley (R-IA), Sherrod Brown (D-OH), Ben Ray Luján (D-NM), Bob Casey (D-PA), and Cindy Hyde-Smith (R-MS) reintroduced the Pharmacy and Medically Underserved Areas Enhancement Act, bipartisan legislation that would authorize Medicare coverage for a broader range of pharmacist services for patients in medically underserved areas in communities that lack easy access to doctors.

The numbers speak for themselves. It's not a field of dreams; patients want health care services from their local pharmacies and pharmacists. Now Congress needs to play ball and build provision of these pharmacist–patient care services into law, and they will come. ■

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Interim Executive Vice President and CEO
American Pharmacists Association

NEW DRUGS

TOFERSEN

(Qalsody—Biogen)

Drug class: Qalsody is an antisense oligonucleotide.

Indication: Qalsody is indicated for the treatment of amyotrophic lateral sclerosis in adults who have a mutation in the superoxide dismutase 1 (SOD1) gene. This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain observed in patients treated with Qalsody. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

Recommended dosage and administration: Qalsody is administered intrathecally. The recommended dose is 100 mg (15 mL) per administration. Treatment should be initiated with three loading doses administered at 14-day intervals. After initiation, a maintenance dose should be administered once every 28 days. Qalsody should be warmed to room temperature before administration occurs and should be administered within 4 hours of removal from vial. Prior to administration, remove approximately 10 mL of cerebrospinal fluid. Administer as an intrathecal bolus injection over 1 to 3 minutes.

Common adverse effects: The most common adverse reactions were pain, fatigue, arthralgia, increased cerebrospinal fluid white blood cell count, and myalgia.

Warnings and precautions: Serious events of myelitis and radiculitis have been reported. Monitor for symptoms. A diagnostic workup and treatment should be initiated according to the standard of care. Serious events of papilledema and elevated intracranial pressure have been reported. Monitor for symptoms and initiate treatment as needed according to the standard of care. Monitor for symptoms of aseptic meningitis and initiate treatment according to the standard of care.

NEW INDICATIONS

ATOGEPANT

(Qulipta—AbbVie)

Drug class: Qulipta is a calcitonin gene-related peptide receptor antagonist.

Indication: Qulipta is indicated for the preventative treatment of migraine in adults.

Recommended dosage and administration: Qulipta is taken orally with or without food. For episodic migraine, the recommended dosage is 10 mg, 30 mg, or 60 mg taken once daily. For chronic migraine, the recommended dosage is 60 mg taken once daily. For patients with severe renal impairment or end-stage renal disease, the recommended dose is 10 mg once daily for episodic migraine. Avoid use for chronic migraine in these patients.

Common adverse effects: The most common adverse reactions are nausea, constipation, and fatigue/somnolence.

Warnings and precautions: Qulipta is contraindicated in patients with a history of hypersensitivity to atogepant or to any of the components of Qulipta. If a hypersensitivity reaction occurs, discontinue Qulipta and initiate appropriate therapy. Severe hypersensitivity reactions have included anaphylaxis and dyspnea. These reactions can occur days after administration. Avoid use in patients with severe hepatic impairment. Based on animal data, use in pregnancy may cause fetal harm. In patients who are concomitantly taking a strong CYP3A4 inhibitor, the episodic migraine dose is 10 mg once daily and use should be avoided in chronic migraines. In patients who are concomitantly taking a strong, moderate, or weak CYP3A4 inducer, the episodic migraine dose is 30 mg or 60 mg once daily and use should be avoided in chronic migraines. In patients taking an OATP inhibitor, the episodic migraine dose is 10 mg or 30 mg once daily and the dose for chronic migraine is 30 mg once daily.

NEW DOSAGE FORMS

ARIPIPRAZOLE

(Abilify Asimtufii—Otsuka Pharmaceutical)

Drug class: Abilify Asimtufii is an atypical antipsychotic.

Indication: Abilify Asimtufii is indicated for the treatment of schizophrenia in adults and as maintenance monotherapy treatment of bipolar I disorder in adults.

Recommended dosage and administration: For patients naive to aripiprazole, establish tolerability with oral aripiprazole prior to initiating treatment with Abilify Asimtufii. The dose should be administered by intramuscular injection in the gluteal muscle by a health care professional. Do not administer by any other route.

Recommended dosage is 960 mg administered once every 2 months as a single injection. Dose can be reduced to 720 mg in patients with adverse reactions. Dosage adjustments may be required if doses are missed. In known poor metabolizers of CYP2D6, the recommended dosage is 720 mg administered once every 2 months as a single injection.

Common adverse effects: The most commonly observed adverse reactions were increased weight, akathisia (an inability to remain still), injection site pain, and sedation.

Black box warning: Older adult patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Abilify Asimtufii is not approved for the treatment of patients with dementia-related psychosis.

Other warnings and precautions: There is an increased incidence of cerebrovascular adverse reactions in older adult patients with dementia-related psychosis. If neuroleptic malignant syndrome occurs, manage with immediate discontinuation and close monitoring. If tardive dyskinesia occurs, discontinue if clinically appropriate. Monitor for hyperglycemia/diabetes mellitus, dyslipidemia, and weight gain. If pathological gambling and other compulsive behaviors occur, consider dose reduction or discontinuation. Monitor heart rate and BP and caution patients with known cardiovascular or cerebrovascular disease and risk of dehydration or syncope. Perform complete blood counts in patients with a history of clinically significant low white blood cell count or a history of leukopenia or neutropenia. Consider discontinuing Abilify Asimtufii if there is a clinically significant decline in white blood cell count in the absence of other causative factors. Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold. Use caution when operating machinery as there is potential for cognitive and motor impairment. Dosage adjustments may be necessary for patients taking CYP2D6 inhibitors, CYP3A4 inhibitors, or CTP3A4 inducers for >14 days. Abilify Asimtufii may cause extrapyramidal or withdrawal symptoms in neonates with third-trimester exposure.

RIZATRIPTAN

(RizaFilm—IntelGenx)

Drug class: RizaFilm is a serotonin (5-HT) 1B/1D receptor agonist.

Indication: RizaFilm is indicated for the acute treatment of migraine with or without aura in adults and in pediatric patients 12 to 17 years weighing ≥40 kg. RizaFilm is not indicated for the preventative treatment of migraine or for the treatment of cluster headache. Use only after a clear diagnosis of migraine has been established.

Recommended dosage and administration: RizaFilm is administered on the tongue. The recommended dosage for adults is 10 mg single dose. Doses should be separated by at least 2 hours and the maximum cumulative dosage in a 24-hour period is 30 mg. The recommended dosage in pediatric patients 12 to 17 years weighing ≥40 kg is 10 mg as a single dose.

Common adverse effects: The most common adverse reactions in adults were asthenia/fatigue, somnolence, pain/pressure sensation, dizziness, and nausea.

Warnings and precautions: RizaFilm is contraindicated in patients with a history of ischemic heart disease or coronary artery vasospasm, history of stroke or transient ischemic attack, Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders, peripheral vascular disease, ischemic bowel disease, uncontrolled hypertension, recent (within 24 hours) use of another 5-HT1 agonist or of an ergotamine-containing medication, hemiplegic or basilar migraine, MAOI use in the past 2 weeks, co-administration with propranolol, or hypersensitivity to rizatriptan or any of the ingredients of RizaFilm. Based on animal data, use in pregnancy may cause fetal harm. Perform cardiac evaluation in patients with multiple cardiovascular risk factors.

Discontinue dosing if arrhythmias occur. Chest/throat/neck/jaw pain, tightness, pressure, or heaviness is generally not associated with myocardial ischemia. Discontinue dosing if cerebral hemorrhage, subarachnoid hemorrhage, or stroke occurs. Discontinue dosing if gastrointestinal ischemic events or peripheral vasospastic reactions occur. Angioedema and anaphylaxis have occurred. If medication overuse headache occurs, detoxification may be necessary. Discontinue dosing if serotonin syndrome occurs.

LACOSAMIDE

(Motpoly XR—Aucta Pharmaceuticals)

Drug class: Motpoly XR is an anticonvulsant.

Indication: Motpoly XR is indicated for the treatment of partial-onset seizures in adults and pediatric patients weighing at least 50 kg.

Recommended dosage and administration: In adults 17 years and older, the initial dosage for monotherapy for the treatment of partial-onset seizures is 200 mg once daily. Initial dosage for adjunctive therapy for treatment of partial-onset seizures is 100 mg daily. The maximum recommended dosage for monotherapy and adjunctive therapy is 400 mg once daily. In pediatric patients weighing at least 50 kg, the initial dosage for treatment of partial-onset seizures is 100 mg once daily. Dosage should be increased based on clinical response and tolerability but should not be increased more frequently than once a week. Motpoly XR capsules should be swallowed whole and can be taken with or without food.

Common adverse effects: The most common adverse reactions in patients taking Motpoly XR include diplopia, headache, dizziness, nausea, and somnolence.

Warnings and precautions: Pregnant patients should be advised that Motpoly XR may cause fetal harm. Dosage adjustments are recommended for severe renal impairment and mild and moderate hepatic impairment. Use in patients with severe hepatic impairment is not recommended. Monitor patients for suicidal behavior and ideation. Obtain an ECG before beginning therapy and after titration to steady-state maintenance in patients with underlying proarrhythmic conditions or on concomitant medications that affect cardiac conduction and closely monitor these patients. Motpoly XR should be gradually withdrawn to minimize the potential of increased seizure frequency. Drug reaction with eosinophilia and system symptoms or multiorgan hypersensitivity may occur and Motpoly XR should be discontinued if no alternate etiology exists. ■

Also in this issue
FDA approves Zavzpret (Pfizer) for the acute treatment of migraine with or without aura in adults (page 19)

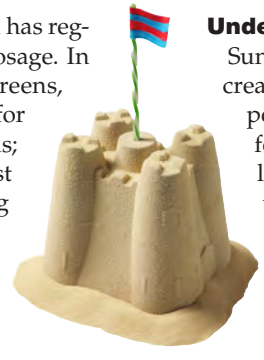
Sunscreen: Preventing sunburn and skin cancer

Mary Warner

Although sun exposure has been known to have damaging effects on skin since ancient times when Egyptians used mixtures thought to prevent sunburn, it wasn't until the late 1800s that the negative health effects of prolonged exposure to UV rays were scientifically confirmed. In 1896, Paul Unna, a German physician, described an association between sun exposure and skin cancer, and in 1910, Unna developed a sunscreen from chestnut extract. Until the 1980s, however, sunscreen use wasn't common, and the first sun protection factor (SPF) 15 sunscreen wasn't introduced until 1986. In recent years, as cases of skin cancer have increased, the safety and effectiveness of sunscreens has garnered much attention.

FDA's role

FDA has regulated sunscreens since the 1970s and has regularly issued guidance about ingredients and dosage. In 2019, FDA issued a new proposed rule on sunscreens, which suggested revisions to the requirements for sunscreen active ingredients; maximum SPF levels; broad spectrum requirements (protection against both UVA and UVB rays); and dosage forms, among other things. The proposed rule also included updates on how sunscreens are labeled to make it easier for consumers to identify key information.



In 2020, before the 2019 rule took effect, the CARES Act replaced the rule-making process with an administrative order process for issuing, revising, and amending OTC monographs, which establish conditions, such as active ingredients, uses (indications), doses, labeling, and testing, under which an OTC drug is "generally recognized as safe and effective" and can be marketed without a new drug application and FDA pre-market approval. The new process allows for revision of monographs as new data become available or emerging safety issues arise.

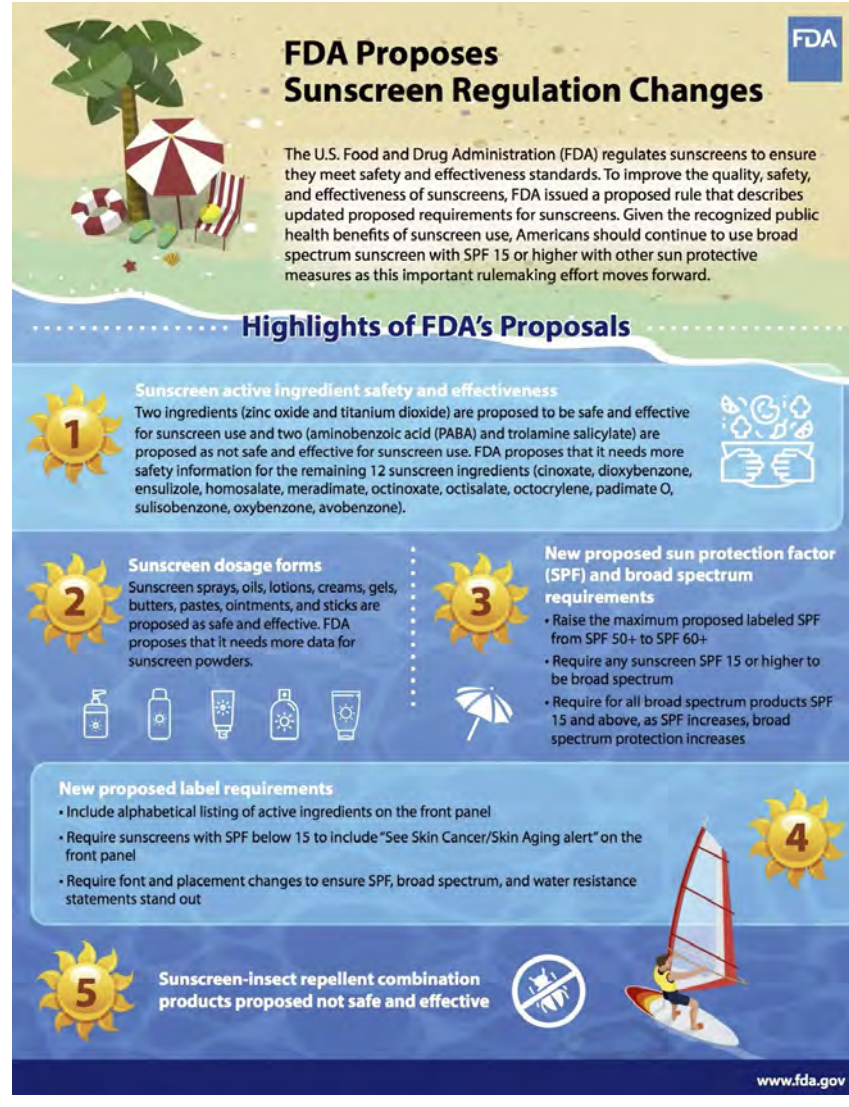
In September 2021, FDA issued a proposed order that transitions several of the proposals in the 2019 regulation, including those pertaining to safe and effective ingredients, dosage forms, SPF and broad-spectrum coverage requirements, labeling requirements, and combination sunscreen/insecticide products to the new order process created by the CARES Act (see infographic).

Understanding sunscreens

Sunscreen comes in many forms, including lotions, creams, sticks, gels, oils, pastes, and sprays. It's important to note that the safe and effective status for spray sunscreens is subject to testing and labeling requirements in the 2021 proposal and that sunscreen sprays should never be applied directly to the face. FDA has not authorized marketing of nonprescription sunscreen products in the form of wipes, towelettes, powders, body washes, or shampoos.

The SPF value of a sunscreen indicates the level of sunburn protection provided, with higher SPF values providing greater sunburn protection. However, because SPF values are determined using a test that measures protection from only UVB radiation, these values only indicate a sunscreen's UVB protection. Beginning in 2011, sunscreens that demonstrate protection against both UVA and UVB radiation can be labeled as "Broad Spectrum SPF [value]."

It's important to choose a suncreen with broad spectrum protection from both UVA and UVB radiation and one with an SPF of at least 15.



It's important to choose a suncreen with broad spectrum protection from both UVA and UVB radiation and one with an SPF of at least 15. Sunscreens that are not broad spectrum or that lack an SPF of at least 15 must carry a warning on the label stating that it has been shown only to help prevent sunburn, not skin cancer or early skin aging.

Two ingredients (zinc oxide and titanium dioxide) are considered to be safe and effective in the 2021 proposed order. Sunscreens that contain the two ingredients (PABA and trolamine salicylate) that are proposed as not safe and effective for sunscreen use and the 12 ingredients for which FDA needs more safety information are still available but should be used with caution.

It's also important to note that in Europe and other areas beyond the United States, sunscreens are regulated as cosmetics rather than as drugs and are subject to different marketing requirements. If a sunscreen is purchased outside the United States, it's important to read the label to understand the instructions for use and any potential differences between it and U.S. products.

Finally, FDA notes that there is no such thing as waterproof sunscreen. Products labeled as "water resistant" must state whether they remain effective for 40 minutes or 80 minutes after swimming or sweating, and all sunscreens must provide clear instructions on when they should be reapplied.

What to tell your patients

Advise patients to choose a sunscreen with an SPF of at least 15, and for those with fair skin, an SPF of 30 to 50 is recommended. Because the SPF is related to the intensity of sun exposure, not the time of exposure, patients should consider time of day as well as geographic location (solar intensity is highest in mid-day and at lower latitudes) when using sunscreen. Time in the sun should be limited between 10 am and 2 pm, with sunscreen applied at least every two hours. Sunscreen should also be used regardless of temperature as harmful UV rays are out year round. Because sunscreens are not recommended for infants under 6 months, these youngest patients should be covered when in the sun. ■

FDA's dietary supplement ingredient directory

Mickie Cathers

On March 6, 2023, FDA released its Dietary Supplement Ingredient Directory, a new way for consumers, manufacturers, and retailers to quickly locate information about products and ingredients marketed as dietary supplements.

This recently unveiled public directory replaces data and information previously scattered across different pages of the FDA website, collating the information in one spot. The supplement ingredient directory is presented in list form with links to FDA's actions and communications for each ingredient on the list and an opportunity to download the data in Excel. You can type an ingredient into the search bar and find other known names for ingredients and related agency actions and statements.

For example, searching for "B12" brings up three product entries linked to a May 2001 agency statement on a settlement reached regarding health claims and bottle labeling. Typing "methylsynephrine," a stimulant found in some weight-loss supplements, into the search box returns four alternate names (oxilofrine, *p*-hydroxyephedrine, para-hydroxyephedrine, and 4-hydroxyephedrine) and two agency actions/statements. The linked actions provide further details and a constituent update revealing that methylsynephrine does not meet the legal definition of a dietary ingredient. FDA considers any product declaring methylsynephrine as a dietary ingredient to be misbranded, and has issued warning letters to seven companies with product labels listing methylsynephrine.

What's in a supplement?

Dietary supplements can contain two types of ingredients: dietary ingredients and other ingredients.

A dietary ingredient is a vitamin, mineral, herb or other botanical, amino acid, or "dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of any dietary ingredient from the preceding categories" as defined by the Federal Food, Drug, and Cosmetic Act.

"Other ingredients" in a dietary supplement are usually listed separately on the facts label and include binders, coloring agents, fillers, flavorings, preservatives, and sweeteners. FDA's new ingredient directory covers dietary ingredients, but not other ingredients within a supplement such as cellulose gel or soybean oil.

FDA's Dietary Supplements webpage provides information for consumers on dietary products and ingredients, including resources, links, and tips for consumers and industry, a way to report adverse events or other problems with dietary supplements, and guidance and background information for industry. Other popular topics include "What's New in Dietary Supplements," safety alerts, and recalls. FDA.gov provides a searchable directory of these, sorted by product type or terminated recall (where FDA has determined all reasonable efforts have been made to remove or correct a product per the recall strategy). They also offer the ability to subscribe to email updates for timely alerts.

While the new ingredient directory doesn't represent a comprehensive list of dietary supplement ingredients and may not include all actions the agency may have taken, FDA will update the directory periodically to reflect new developments. FDA also encourages additional feedback and information regarding ingredients, which can be submitted to FDA's Office of Dietary Supplement Programs at ODSP@fda.hhs.gov.

FDA's new ingredient directory covers dietary ingredients but not binders, coloring agents, fillers, flavorings, preservatives, and sweeteners.

Regulating supplement and ingredients

FDA regulates both finished dietary supplement products and dietary ingredients under a different set of regulations than those covering conventional foods and drug products. Per the Dietary Supplement Health and Education Act (DSHEA) of 1994, FDA's responsibility is to take action against adulterated or misbranded dietary supplements after, not before, they reach market shelves. DSHEA places responsibility for safety and labeling evaluation of products on manufacturers and distributors, not on FDA. It is the manufacturer that must ensure they meet all DSHEA and FDA regulations and requirements. ■

Zavzpret: New option for migraine sufferers

Lauren Howell, PharmD

In March of this year, FDA approved the first and only calcitonin gene–related peptide (CGRP) receptor antagonist nasal spray for the acute treatment of migraine with or without aura in adults. This approval is a major breakthrough for individuals with migraine who prefer not to use oral medications.

Recommended dosage and how it works

Zavzpret (zavegepant–Pfizer) is a CGRP receptor antagonist, but the relationship between pharmacodynamic activity and the mechanism by which zavegepant exerts its clinical effects is unknown. While indicated for the acute treatment of migraine, it should not be used for the preventative treatment of migraine. The recommended dose is 10 mg given as a single spray in one nostril as needed. The maximum dose in a 24-hour period is 10 mg, so no more than one spray should be administered in that time frame. The safety of treating more than eight migraines in a 30-day period has not been established.

Adverse effects

Use of Zavzpret is contraindicated in patients with a history of hypersensitivity reaction to zavegepant or to any of the components of Zavzpret. If a serious hypersensitivity reaction occurs, discontinue Zavzpret and initiate appropriate therapy. Reactions including facial swelling and urticaria have occurred. The most common adverse reactions in patients being treated with Zavzpret were taste disorders, nausea, nasal discomfort, and vomiting. Avoid use with drugs that inhibit or induce OATP1B3 or NTCP transporters. Avoid use of intranasal decongestants; if this is unavoidable, administer intranasal decongestants at least 1 hour after Zavzpret administration. Avoid use in patients with severe hepatic impairment and with a creatinine clearance of <30 mL/min.

Clinical trials

The efficacy of Zavzpret for the acute treatment of migraine with or without aura in adults was demonstrated in two randomized, double-blind, placebo-controlled trials. In both studies, patients were instructed to treat a moderate to severe migraine with Zavzpret. Other medications such as NSAIDs, acetaminophen, or an antiemetic were allowed to be used as long they were administered 2 hours after the initial treatment with Zavzpret. Other forms of rescue medications such as triptans were not allowed during the 48 hours following initial treatment.

In both studies, patients were randomized and either received a single dose of Zavzpret or placebo. Efficacy was demonstrated with Zavzpret 10 mg by an effect on the coprimary endpoints of pain freedom and most bothersome symptom freedom at 2 hours after a single dose, compared to placebo. The percentage of patients achieving headache-pain freedom and most bothersome-symptom freedom 2 hours after a dose was statistically significantly greater in patients who received Zavzpret than those who received placebo.

The maximum dose in a 24-hour period is 10 mg, so no more than one spray should be administered in that time frame.

Patient counseling

Patients should be counseled on the correct way to administer Zavzpret. Each device delivers a single dose and provides one spray that should be delivered into one nostril. The device contains a spray nozzle that should be inserted into the nose and a plunger that to be pressed with the thumb.

Patients should not remove the device from the blister packaging until they are ready to use it. The device should not be primed, and the plunger should not be pressed before dosing. If the plunger is pressed prior to administration, the spray will be lost and the device will no longer function.

Patients should be advised not to spray a dose into more than one nostril, as only one dose should be used in 24-hour period. Patients should be advised to gently blow their nose before administering the dose. Once the dose is administered, it is important that the individual keeps their head level and upright for 10–20 seconds. If the patient feels a drip from their nose, they should gently sniff so that none of the dose is lost. After administration, the used device should be thrown away. ■

Treatment for Alzheimer disease in flux

Mickie Cathers

When the latest drugs to treat Alzheimer disease are expensive, hard to get, and backed with little evidence, how do pharmacists and other clinicians help patients?

Alzheimer disease affects more than 6.7 million Americans. Due to the nature of this neurodegenerative condition, treating it is much broader than prescribing medications.

"It's a win if the patient doesn't feel different. But how do you explain to a patient that they are 6 to 12 months 'better' than where they were predicted to be? People need to understand that you don't 'go back to your old self.'"

"Progression of cognitive impairment starts to go downhill after our mid to late 20s," said Jeff Sherer, PharmD, MPH, clinical professor at the University of Houston College of Pharmacy. In his talk at APhA2023 in March, Sherer said, "[s]ome people lose some cognitive function but might never hit the level of mild cognitive impairment, which is not dementia. And others might find they've progressed through mild cognitive impairment into Alzheimer disease. These designations come into play regarding who gets prescribed medication."

Current treatment options for Alzheimer disease include pharmacological and nonpharmacological methods.

Pharmacological approaches

There are only a handful of FDA-approved drugs available, including cholinesterase inhibitors (ChEIs), memantine, aducanumab, and lecanemab.

ChEIs—that is, donepezil, rivastigmine, and galantamine—are still first-line treatments for patients as they help with symptoms. They are generally well-tolerated and come in varying dosages. ChEIs have been shown to slow the advancement of symptoms of Alzheimer disease by the equivalent of 6 to 12 months.

ChEIs inhibit acetylcholine turnover and restore synaptic levels of this neurotransmitter. Acetylcholinesterase inhibitors are known for being the most effective, but a patient needs to take the drug four times a day, which isn't easy for someone struggling with memory issues. They can also adversely affect the liver.

"Alzheimer disease is a progressive condition," said Sherer. "It's a win if the patient doesn't feel different. But how do you explain to a patient that they are 6 to 12 months 'better' than where they were predicted to be? People need to understand that you don't 'go back to your old self.'"

Memantine, an *N*-methyl-D-aspartate receptor antagonist, is an excitatory that FDA approved in October 2003 for moderate to severe Alzheimer disease. While this drug is well-tolerated by patients and can be used with

donepezil, it's unclear from the data how effective it is.

Changing landscape

In 2018, Pfizer announced it was abandoning research into new drugs aimed at treating Alzheimer disease. "This was a big deal in the Alzheimer disease community and set the stage for the two new amyloid β-directed monoclonal antibodies, aducancumab and lecanemab," said Sherer.

Aducancumab addresses inflammation and memory loss and is given to patients by I.V. every 4 weeks for the treatment of mild cognitive impairment. Its approval was based on two studies showing a reduction in amyloid β plaque.

However, not only is there insufficient evidence of meaningful clinical benefit for patients, but significant adverse effects, including cerebral edema in 35% of patients and microhemorrhage in 19% of patients, have been reported. MRIs are required at baseline and before the seventh and twelfth doses, per FDA labeling.

Today, many health care providers focus the most on caregiver support for patients with Alzheimer disease and dementia.

Lecanemab is similar to aducanumab. Approved on January 6, 2023, for mild cognitive impairment and mild dementia, and administered by I.V. every 2 weeks, this drug presents insufficient evidence of clinical benefit and significant adverse effects.

Sherer has concerns about the adverse effects, but also about access issues to these drugs.

At this time, Medicare generally only covers both of these drugs as part of a clinical trial, and with the high price tag these newer agents may be out of reach for many patients.

"Since CMS is basically only paying for the newer drugs in the setting of a clinical trial, that's the only way most patients have even a possibility of accessing them," said Sherer.

The Alzheimer's Association has a service named Clinical Trial Match available at: www.alz.org/alzheimers-dementia/research_progress/clinical-trials/trialmatch.

Nonpharmacological approaches

"Nonpharmacologic approaches are way more helpful than the drugs available today," said Sherer.

Today, many health care providers focus the most on caregiver support for patients with Alzheimer disease and dementia.

These methods might include nonconfrontational redirection, environmental modification (e.g., turning off the gas to the house), and distraction such as giving the patient a way to focus energy on things that won't harm them.

Written reminders, pet therapy, and reminiscence therapy are also helpful. Short-term memory is what goes first, and so talking with the patient about what they can remember from the past provides comfort as well as going through photo albums together.

Future directions

While research on better drugs, earlier identification, and prevention continue, health care providers can still do a lot to help their patients with Alzheimer disease and their caregivers using both nonpharmacological and pharmacological treatments together.

"Right now, we study patients at the curve from mild cognitive decline into Alzheimer disease, but we should be looking earlier," said Sherer. "Plaque starts forming in your 40s and 50s. Should we look at that age group? Those are the patients who will clearly benefit. How do you operationalize this? Make them get an MRI once a year? Ask them to start a $56K/day drug now?" ■

Fatal opioid poisoning in children skyrockets

Shivani Modi, PharmD

Opioid poisoning is the leading cause of fatal poisoning in young children, according to new research published March 8, 2023, in *Pediatrics*.

Researchers wanted to investigate and understand the factors that contribute to fatal poisoning in the pediatric population. Using data from the National Fatality Review Case Reporting System, the research team analyzed factors related to poisoning among children ages 5 years and younger from 2005 to 2018.

During the study period, 731 poisoning-related cases were reported in children. Among all the cases reported, over three-fifths of poisoning fatalities occurred in a child's home and approximately one-third occurred while they were supervised by an adult other than a biological parent. In 2018, researchers found that opioid poisonings accounted for over half of all poisoning fatalities in children.

Overall, opioid poisoning-related death rates have increased from 24% in 2005 to 52% in 2018, according to the findings.

These children were exposed to illicit opioids such as heroin and fentanyl as well as opioids used in medication-assisted treatments like methadone and buprenorphine.

Researchers found that OTC pain, cold, and allergy medications also contributed greatly to deaths in this population. They found that 74% of poisoning-related fatalities for children 2 years and younger were due to OTC pain medications. In the pediatric population, poisoning prevention is critical.

Parents and caregivers must take appropriate measures such as using correct dosing and administration to prevent adverse outcomes.

Counseling

In addition to appropriate labeling on OTC medications, pharmacists and clinicians can help by counseling parents and caregivers on correct dosing and techniques to administer OTC medications to children.

Pharmacists can counsel parents and caregivers on home safety, including storing medications in the original container and/or cabinets, off-label use of OTC medications, and the importance of using age-appropriate and weight-based dosing that can prevent fatal poisoning.

Pharmacists should be trained to recognize opioid overdose symptoms, such as altered mental status or respiratory depression, and indications for the use of naloxone. Pharmacists should also have strategies in place to mitigate such complex situations and identify early signs to provide comprehensive education to parents and caregivers.

Preventing fatal opioid poisoning requires that pharmacists and other health care professionals ensure the safety of patients through counseling and education about the dangers of opioids.

In addition, pharmacists should offer community interventions and resources if parents and caregivers demonstrate a lack of understanding due to contributing social determinants of health.

Context

Findings from the study are in line with previous studies that demonstrate increased rates of pediatric deaths related to opioid poisoning.

Earlier studies showed opioids, antihistamines, and sympathomimetics as common agents that contributed to fatal opioid poisoning in children. Authors of the study also note that policymakers and programmatic initiatives should focus on the types of opioids circulating during the ongoing epidemic as it relates to children living with adults.

In this study, researchers emphasize that despite the precautions and measures taken by the regulatory agencies to have improved labeling on OTC products as well as unit dose packaging to reduce fatal opioid poisoning, this does not include all medications such as prescription drugs and opioids. They said that further interventions need to be put in place to reduce poisoning in the pediatric population, and strategies should be developed to educate all health care professionals as well as parents and caregivers.

"A subset of our study population demonstrated factors associated with child abuse, including history of previous maltreatment, illness or disability, or sibling placement," the authors wrote. "Other familial and community factors, including substance use disorder, poverty, and social inequities, have been identified as associated factors. Further research is needed to elucidate the role of these social factors in fatal poisoning to inform individual- and community-level safety interventions." ■

Reproductive health and COVID-19: Dispelling misinformation

Clarissa Chan, PharmD

A January 10, 2023, article in *JAPhA* provides counseling points for pharmacists who are trying to help their patients of reproductive age with the questions and concerns they may have related to COVID-19 and COVID-19 vaccines in this time of misinformation and disinformation.

"All health care professionals must gain the public's trust within their communities to dispel myths," said Veronica Vernon, PharmD, BCPS, BCACP, assistant professor of pharmacy practice at Butler University in Indianapolis, IN, who contributed to the article.

"Pharmacists are among the most well-positioned providers to build and nurture trusting relationships with patients, connecting them with health care—including sexual and reproductive—services," said Megan N. Freeland, PharmD, director of health communications at Planned Parenthood Federation of America in Atlanta, GA.

The following are commonly asked questions to help pharmacists best guide their patients on the impact of the COVID-19 infection and vaccines on reproductive health care.

Do COVID-19 infection and/or vaccines affect menstrual cycles?

"Recent research shows that COVID-19 infection [and] vaccines may affect a person's menstrual cycle," said Camille Clare, MD, MPH, FACOG, professor of obstetrics and gynecology at SUNY Downstate Medical Center in Brooklyn, NY. "Some reported adverse effects are lighter, heavier, or irregular periods." Changes are usually temporary, and most people return to their normal cycles 1 to 2 months after vaccination.

"The benefits of getting vaccinated against COVID-19 outweigh any risks of temporary changes to a person's menstrual cycle," said Clare.

Does getting the COVID-19 vaccine cause infertility?

Getting a COVID-19 vaccine won't impact your fertility, but getting the virus could, according to Clare. "Becoming infected with the coronavirus may affect the quality and quantity of sperm. Getting vaccinated against COVID-19 is a safe and effective way to protect against severe illness and may protect sperm."

The American College of Obstetricians and Gynecologists and CDC recommend COVID-19 vaccination for those planning to get pregnant. "Don't wait to get vaccinated. The COVID-19 vaccine is safe and effective for couples planning to conceive and undergoing fertility treatments," she said.

"Don't wait to get vaccinated. The COVID-19 vaccine is safe and effective for couples planning to conceive and undergoing fertility treatments."

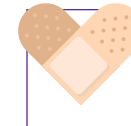
Can COVID-19 vaccines affect a pregnancy or pregnant people?

"COVID-19 vaccines are safe and effective for pregnant [and lactating] people. Pregnant people are more likely to get severely ill from COVID-19. Getting vaccinated can help prevent severe illness, hospitalizations, and death," said Clare.

Breast milk provides babies with antibody protection against many illnesses, including COVID-19. The benefits of breastfeeding outweigh any potential risks, and there is no evidence that the coronavirus passes through breast milk.

Can COVID-19 infection increase blood clot risk?

Clare noted that a COVID-19 infection causes widespread inflammation affecting how well blood cells work, and may cause abnormal blood clotting. ■



APhA offers counseling points for pharmacists at apha.us/PregnancyFertility

Myth and misinformation NOTHING NEW

Sonya Collins

IN THE SPRING OF 2021, protesters gathered outside Sentinel High School in Missoula, MT. They waved signs and held out flyers that claimed the COVID-19 vaccine caused miscarriage and infertility. They screamed "baby killer" at every parent and student who rushed by on their way inside to the vaccine clinic.

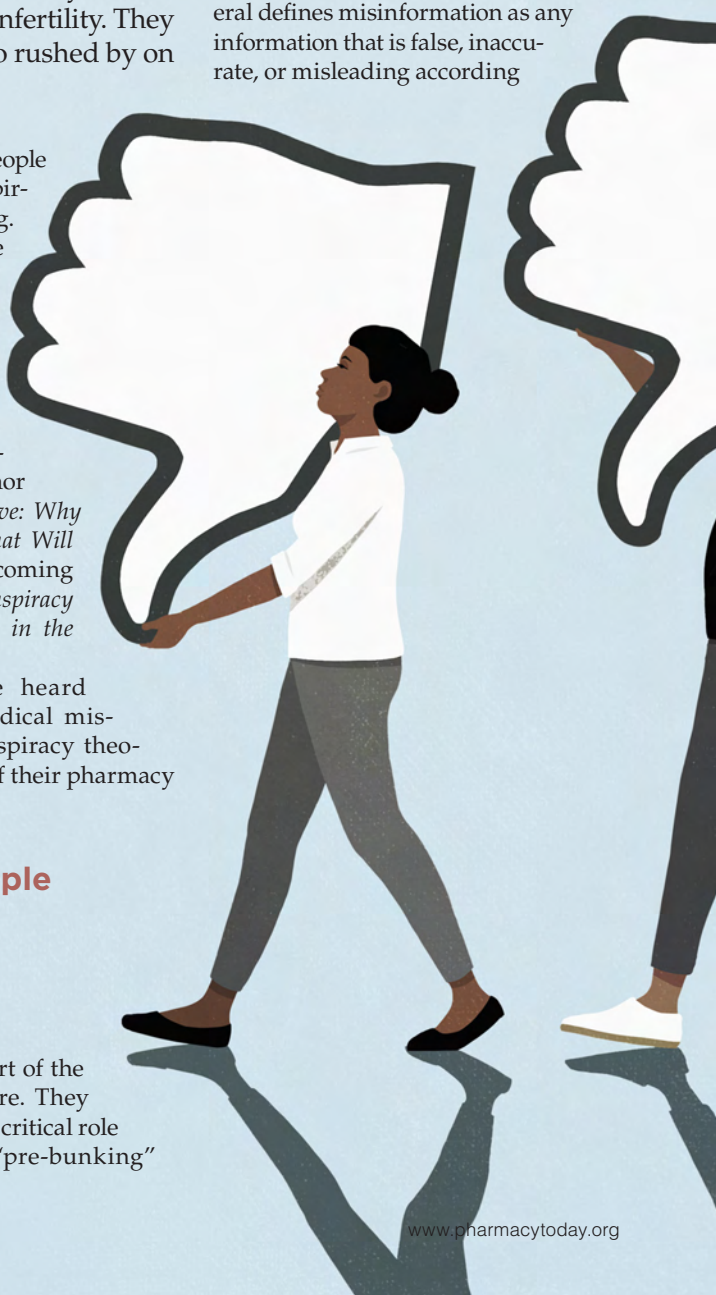
When clinic staff learned what was going on outside, they sent a mass text to everyone who'd scheduled an appointment for that day and advised them to keep their windows up until they parked and to come directly inside to the gym.

The infertility myth started making the rounds on social media almost as soon as the first COVID-19 vaccine became available. Alongside it were numerous other falsehoods that ranged from simple misunderstanding (e.g., the vaccine didn't go through safety and efficacy testing) to conspiracy theories (e.g., the vaccines contain a microchip).

While medical misinformation and pseudoscience have been around for longer than the COVID-19 virus, the pandemic arguably exacerbated the problem.

Misinformation, disinformation

The Office of the U.S. Surgeon General defines misinformation as any information that is false, inaccurate, or misleading according



trol—that can make people double down on conspiratorial-style thinking. The problems were definitely already there, but it might have been easier for people to grasp onto misinformation in the pandemic," said Sara Gorman, PhD, MPH, author of *Denying to the Grave: Why We Ignore the Facts that Will Save Us* and the forthcoming *Modern Medicine: Conspiracy Theories and Distrust in the 21st Century.*

Pharmacists have heard claims based on medical misinformation and conspiracy theories from both sides of their pharmacy

Medical misinformation can dissuade people from getting necessary health care in a timely manner or at all.

"There were a number of things about that pandemic—so much uncertainty, some communication missteps on the part of the government and CDC, and people feeling a loss of control

counters since the start of the pandemic—and before. They can continue to play a critical role in debunking and "pre-bunking" these harmful myths.

to the best available evidence at that time. While some misinformation may be borne out of an earnest mistake or misunderstanding, some falsehoods—called disinformation—are knowingly fabricated and perpetuated.

"Whether it's innocent or a coordinated, targeted sharing of misleading ideas, it's hard to know anyone's intent, especially online, so we need to have a multipronged strategy to tackle all of it," Gorman said.

Terrified of contracting and dying of COVID-19, people were willing to believe in unfounded claims about treatments, cures, or preventatives. Others leaned on denial of the scope of the pandemic altogether.

Effects of medical misinformation

Misinformation has numerous channels through which to travel. Social media and messaging apps are among the most robust. But with the increasingly widespread consumption of preprints during the pandemic, the mainstream media also fell prey to research findings

based on flawed study designs or insufficient data.

In early 2020, a paper appeared on preprint server BioRxiv claiming that there were "uncanny" similarities between COVID-19 and HIV and implying that the virus might be man-made. The paper was removed from the server quickly but may have already had untold views.

Then misinformation hit social media, where there is no reeling it back in.

Research shows that the public is more likely to engage with misinformation than factual information, and that negative misinformation is harder to neutralize than positive.

Its effects are far-reaching, too. Medical misinformation can dissuade people from getting necessary health care in a timely manner, or at all. It can spur vaccine hesitancy, medication noncompliance, disease outbreaks, hospitalization, and even death.

Multiple studies in relation to COVID-19 and other vaccines have shown that exposure to misinformation weakens intent to receive vaccines.

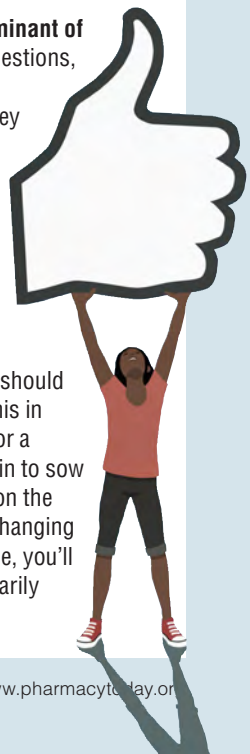
In a 2014 study in *PLOS One*, participants were exposed to information that either supported or refuted an antivaccine conspiracy theory or a control condition. After exposure, they were asked to rate their intent to vaccinate a hypothetical child. Those who had seen the antivaccine conspiracy theory were less likely to have a child vaccinated.

In a 2021 randomized controlled trial published in *Nature Human Behavior*, a total of 8,000 participants (half in the United Kingdom, half in the United States) were asked about their intent to

What pharmacists can do

Pharmacists are at the frontlines of the battle against misinformation. Over the course of the pandemic, and long before that, they have fielded numerous misinformation-based questions. Here are best practices for addressing these myths and misunderstandings:

- **Pre-bunking is better than debunking.** Once a person has been exposed to misinformation, even when it's later corrected, it can be very difficult to disabuse the person of that belief.
- **Some organizations are exploring ways to surveil misinformation and create pre-emptive messaging to debunk it.** Ideally, there would be a system for this. Until that time, pharmacists could inoculate their patients and communities against rumors they hear. "In the waiting room at the pharmacy, there could be signs or videos that say, 'You might hear this about the COVID vaccine, and here's how people will try to convince you that's true,' and then you could debunk it," said Sara Gorman, PhD, MPH.
- **Check your own biases.** Anyone can be swayed by a myth or pseudoscience. Pharmacists should approach conversations with patients who believe false claims with an open mind. "When a patient shares misinformation, that doesn't mean they are uneducated," Gorman said. "It doesn't say anything in particular about that individual."
- **Listen first.** Before pharmacists start to counter the misinformation with fact, they should listen to understand why the patient believes the false information and where they might have learned it. "The number-one lesson we learned from the pandemic is to always listen. Listening and empathy come first," Gorman said. "There is no conversation if it starts with an adversarial tone."
- **Ask open-ended questions.** Pharmacists can gain the trust of patients and better prepare themselves to counter misinformation when they ask open-ended questions. Ask why the patient believes what they do. Ask where they heard or read that information.
- **Ask for permission to share your own thoughts.** Pharmacists can continue to build trust by asking for permission to share facts that counter the patient's beliefs rather than simply correcting the patient.
- **Present information in a convincing way.** Use stories, examples, and analogies as much as possible. These may stick with people better than data do. "You can tell someone a statistic from a study, but it may not mean as much as concrete examples," said Chana Davis, PhD. "Even though it's less scientifically rigorous, if it helps communicate your message, it's worth doing."
- **Point patients toward credible sources.** Whether or not pharmacists can change a patient's mind in a single exchange, they can make patients aware that their sources of misinformation are not the same sources health care professionals use. "You might say, 'Unfortunately, those concerns are misinformed. That's not a credible source. Can I tell you about the resources we rely on as pharmacists?' " Davis suggested.
- **Consider misinformation as a social determinant of health.** Along with other health screening questions, pharmacists can ask patients where they get health information and probe to learn why they hold certain beliefs. "You can then target your recommendations for them," Gorman said, "If they want further information, for example, you could suggest things they could read from the types of sources they would trust."
- **Play the long game.** Often, it takes more than one encounter to change the mind of a patient who holds false beliefs. Pharmacists should approach conversations with patients with this in mind. A patient might not roll up his sleeve for a vaccine that day, but the pharmacist can begin to sow the seeds of doubt in whatever misinformation the patient has shared. "You're not necessarily changing minds on the spot," Davis said. "But with time, you'll change a lot of minds. You just won't necessarily see it in every interaction." ■



get a COVID-19 vaccine. Among those in the U.K., 54% planned to receive the vaccine and 42% of Americans did. But after exposure to vaccine misinformation, each group saw a drop in intent of about six percentage points.

Pseudoscience claims can lead people to rely on unproven alternative medicine and forgo conventional medicine altogether.

A 2022 study in the *Journal of the National Cancer Institute* found that 32% of the 200 most popular cancer-related articles shared on social media contained misinformation and 30% of the articles—nearly 77% of those containing any type of misinformation—contained harmful misinformation. User engagement with misinformation was greater than with factual articles, and harmful misinformation garnered the most engagement.

Misinformation and disinformation may also exacerbate existing health disparities as, according to a recent article in the *Journal of the American College of Clinical Pharmacy (JACCP)*, it hits underserved populations the hardest. That includes patients who are Black, LGBTQ+, digitally disadvantaged, or who have lower health literacy.

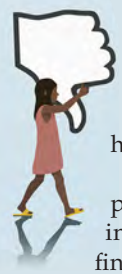
"Marginalized populations may be more prone to believing misinformation due to historical distrust of government or organized associations. They may distrust the health care system, for example, due to past experiences with discrimination," said Micheline Goldwire, PharmD, a professor and director of drug information at Regis University in Denver, CO, and coauthor of the *JACCP* paper. "As far as health literacy, people who are less adept at searching the Internet may be more vulnerable."

No one is immune

Members of marginalized groups might be especially prone to accept misinformation as fact due to feelings of disenfranchisement.

A 2014 study in *PLOS One* found that belief in anti-vaccine conspiracy theories was a strong predictor of feelings of powerlessness, disillusionment, and mistrust in authorities.

Members of marginalized groups are not the only people who may be susceptible to believing medical misinformation.



A number of factors can cause anyone to lower their defenses against false claims about health or science.

People might be more prone to believing misinformation when they find themselves in a distressful situation that does not have a medical explanation or solution.

The COVID-19 pandemic has been the most recent and universally understood example of this. Terrified of contracting and dying of COVID-19, people were willing to believe in unfounded claims about treatments, cures, or preventatives. Others leaned on denial of the scope of the pandemic altogether.

In October 2021, more than two-thirds of Americans believed or were unsure about at least one of eight false statements about the COVID-19 pandemic or COVID-19 vaccines. Among the eight statements were claims that the government was exaggerating the number of COVID-19 deaths, that the vaccine causes infertility, and that pregnant women should not get the vaccine.

Individual circumstances, too, such as infertility or a serious diagnosis with an unknown cause or no cure, can push anyone to grasp onto unfounded explanations or solutions.

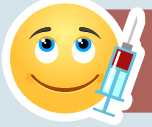
"When something negative happens and you're looking for a solution. You start to ask yourself, 'What did we do before my child got this diagnosis?'" said Chana Davis, PhD, founder of Fueled by Science and contributor at Those Nerdy Girls.

This might explain why people are drawn into false claims about childhood vaccines, since children may receive these around the same time that signs of developmental delays commonly arise.

No one is immune to believing and spreading false information. Even medical professionals buy into and share misinformation with patients or via social media. The problem became so apparent during the pandemic that the American Medical Association has developed policies and protocols for addressing it. Pharmacists interviewed for APhA's Vaccine Confident initiative have shared that members of their own staff, including fellow pharmacists, were reluctant to receive the vaccine due to false beliefs about its safety profile.

"It's important to be humble and recognize in ourselves that we all have a tendency to overweight our own beliefs as correct or to underappreciate how often we are wrong ourselves and the extent to which our decisions have an emotional component to them."

"It's important to be humble and recognize in ourselves that we all have a tendency to overweight our own beliefs as correct or to underappreciate how often we are wrong ourselves and the extent to which our decisions have an emotional component to them," Davis said. ■



APhA offers resources to address misinformation and disinformation surrounding COVID-19 at apha.us/Misinformation

Xylazine worsens overdose rates, threatens harm reduction efforts

Loren Bonner

As if the opioid epidemic in America couldn't get any worse, a new "emerging drug threat" is contributing to the rise in overdose deaths around the country.

In a March 2023 alert, DEA said that it had detected xylazine—a sedative approved for veterinary use—in nearly a quarter of the fentanyl samples confiscated last year in 48 states. In Philadelphia, where illicit drugs containing xylazine have been prevalent for years, the Philadelphia Department of Public Health reported that 90% of sampled street opioids contained xylazine in 2021.

Rahul Gupta, MD, director of the White House Office of National Drug Control Policy, said that "[t]his is the first time in the nation's history that a substance is being designated as an emerging threat by any administration."

Xylazine, which is not approved for human use, is an α_2-andrenergic agonist, similar to dexmedetomidine and clonidine. The xylazine-fentanyl combination depresses an individual's breathing, heart rate, and blood pressure, and can cause wounds that often lead to amputation.

The primary effect of xylazine is profound sedation that is not reversible by naloxone, according to Jeffrey Bratberg, PharmD.

"Naloxone should [still] be given for any suspected overdose, but the goal should be to return to breathing, not consciousness," said Bratberg, a clinical professor of pharmacy practice at University of Rhode Island College of Pharmacy. "Patients should be monitored until the sedation wears off, for up to 4 hours."

Frank Franklin, PhD, JD, MPH, deputy commissioner of health at the Philadelphia Department of Public Health, said they have updated their overdose reversal training with information on xylazine and the complications it may cause during overdose reversals. They are also including wound care in harm reduction efforts.

"Treatment of xylazine withdrawal may require inpatient monitoring for vital sign instability and benzodiazepine tapers," said Franklin. "Co-occurring xylazine and opioid withdrawal can be managed with α_2-adrenergic agonists and pain, insomnia, and anxiety management."

Franklin said pharmacists and other health care providers should continue to provide individuals with access to naloxone and buprenorphine.

Supply

Back in February 2023, FDA said that they were taking action "to restrict the unlawful entry of xylazine active pharmaceutical ingredients and finished dosage form drug products into the country to address a growing public health concern." According to the agency, members of FDA's field staff are being directed to screen all shipments of xylazine being imported into the U.S. in its raw or finished form, to verify that it is properly labeled and en route to legitimate supply chains for veterinary use.

As this story went to press, FDA spokesperson Siobhan DeLancey said it is not known whether the xylazine used in these scenarios is illicitly produced or diverted from the animal drug supply.

Pharmacists who work in compounding facilities should have reasonable certainty that the drugs they are dispensing are intended for legitimate animal use and not going into illicit human drug supply, DeLancey said.

Pharmacy compounders should also be familiar with the circumstances under which FDA will consider enforcement discretion with respect to compounded xylazine products, as outlined in Guidance For Industry #256, which covers compounding animal drugs from bulk drug substances.

Policy implications

Maritza Perez Medina, director of the Office of Federal Affairs at the Drug Policy Alliance, said the current administration should not be pushing more supply-side interdiction policies.

"They are incredibly counterproductive and lead to a more unknown and potentially more potent drug supply," she said in a press release. "Crackdowns on prescription opioids and heroin created the conditions for fentanyl analogues to flourish and overtake the drug supply. And now history is once again repeating itself, with newer, potentially more harmful substances—like xylazine—popping up and already overtaking some markets. Make no mistake, focusing on supply-side interdiction will only dig us deeper into this crisis and inevitably result in more loss of life."

In March 2023, a bill to regulate xylazine under Schedule III of the Controlled Substances Act was introduced in Congress. Putting the drug in this category would criminalize distribution of xylazine for human use.

Veterinarians, in particular, fear that if that happened, their access to the medicine would be heavily regulated, and that production of a classified drug would require additional quality control and security measures that could adversely affect cost and production of the drug. ■

2023 Immunization Champion Awards recognize significant contributions to vaccinations and public health

Pharmacists have long been recognized for the vital roles that they play in delivering vaccines and providing education to patients in their communities.

Pharmacists, in collaboration with physicians, public health officials, and other immunization health partners, are recognized as important members of the immunization neighborhood and are developing solutions to increase access to vaccines and other public health services.

Millions of vaccines are administered by pharmacists each year, and the COVID-19 pandemic has spotlighted the significance of the profession's contributions to public health.

The profession's dedication to meeting the public's immunization needs and protecting people from vaccine-preventable diseases is evident in the work of this year's nominees and the many thousands of immunizing pharmacists practicing in communities nationwide.

To celebrate the achievements of immunizing pharmacists, APhA's Immunization Champion Awards recognize pharmacists, organizations, members of the pharmacy profession, and their allies who have made extraordinary contributions to increase vaccination rates in their communities.

The 2023 Immunization Champions, honored in March 2023 at the APhA Annual Meeting & Exposition in Phoenix, have pioneered new approaches to increasing vaccination rates.

This year's program was supported by CDC; GSK; Merck, Sharp & Dohme; Moderna; Pfizer; and Sanofi/Vaxserve.

Congratulations to all the award recipients!

Individual practitioner

These individuals exemplify pharmacists' impact on patient care and positively portray the value of pharmacists' public health activities.

National Winner

Chichi Ilonzo Momah, PharmD, RPh
Springfield Pharmacy & Medical Supply, Springfield, PA

Chichi Ilonzo Momah, PharmD, RPh, is a graduate of Temple University's School of Pharmacy and has owned the Springfield Pharmacy in Springfield, PA, since 2012.

During the shortage of the new shingles vaccine in 2018, Momah partnered with a vaccine manufacturer to gain access and was the only pharmacy to stock the vaccine across multiple counties in her area.

Momah made waves in the spring of 2021 when her pharmacy was chosen as one of the first sites in Delaware County—the largest county in the nation without a public health department—to administer the COVID-19 vaccine. Momah and the team at Springfield Pharmacy's support of the COVID-19 vaccine rollout were featured locally and nationally, from HHS, Philadelphia's FOX29, NBC Nightly News, the Philadelphia Inquirer, and National Public Radio News.

Momah serves as a luminary to the Pennsylvania Pharmacy Care Network and as an advisory board member to the Elevate Pharmacy Services Administrative Organization and The Freckled Strawberry organizations. She is currently the only approved Vaccine For Children (VFC) pharmacy provider in the state of Pennsylvania.

She also partners with the Department of Health, local health departments, local community leaders, and various long-term care facilities to address vaccine hesitancy and run vaccine clinics.

Through her work—which she says is driven by her care philosophy of "leading with love"—Momah has proven that pharmacists are problem solvers, leaders, and above all, critical patient advocates.

Honorable Mention

Bridget Ogden, PharmD
Cub Pharmacy

Bridget Ogden, PharmD, received her doctorate degree from Creighton University School of Pharmacy and Health Professions in Omaha, NE. She is currently the clinical point person for Cub Pharmacy and serves as the primary preceptor for the Cub Pharmacy PGY-1 Residency Program. In this role, Ogden spearheads vaccination clinic efforts for Cub Pharmacy in the Twin Cities and greater Minnesota area.

Ogden works to coordinate and schedule over 250 influenza vaccination clinics each year and added another 350 COVID-19 vaccination clinics in 2022.

Her most notable effort in the past 12 months is the partnership she forged with multiple pediatrician practices in the Twin Cities area. When the monovalent Pfizer vaccine for ages 5–11 years was going through the authori-

zation process, Ogden started conversations with several pediatricians' offices regarding their plans to vaccinate their patients. When it became clear that many well-established and successful pediatrician practices did not have the staffing resources to vaccinate this population in a timely fashion, Ogden partnered Cub Pharmacy with three pediatric clinic groups. Cub pharmacists and other credentialed immunizers went to the pediatric clinic to administer vaccinations in their exam rooms and spaces.

For the first round of first dose events alone, Ogden and other Cub Pharmacy immunizers vaccinated 1,500 children who otherwise would have experienced delayed access.

Honorable Mention

Renee Robinson, PharmD, MPH, MSPharm, MBA

Idaho State University, College of Pharmacy, Pocatello, ID

Renee Robinson, PharmD, MPH, MSPharm, MBA, completed her doctorate in pharmacy at the University of Georgia and a fellowship in clinical research through NIH; she also has a degree in pediatric pharmacotherapy, and master's degrees in epidemiology and in patient safety.

From 2002 to 2006, she conducted research as faculty in the Department of Pediatrics at Idaho State University (ISU), studying medication adherence and decision-making. In 2008, Robinson joined the United States Public Health Service (USPHS) conducting health research with and for tribal communities in Alaska. In 2018, she joined University of Alaska Anchorage/ISU College of Pharmacy as an associate professor pursuing external research funding to address health disparities through health technology.

Robinson has received many professional awards, including USPHS Junior Pharmacist of the Year, Distinguished Alaskan Pharmacist Award, and *Pharmacy Times* Educator of the Year, and she has worked on a number of immunization efforts such as the Pediatric Ebola Vaccination Trial in Liberia, the Assisted Living Home Immunization event in Alaska, ProjectPak efforts to vaccinate children in the HeadStart program, and partnering with the Navigators to support public health and pharmacy immunization initiatives.

Community outreach

This award recognizes individuals who have made substantial progress in improving the health of their communities.

National Winner

Kevin W. Cleveland, PharmD, ANP

Idaho State University College of Pharmacy, Pocatello, ID

Kevin W. Cleveland, PharmD, ANP, is an associate professor in the Department of Pharmacy Practice at ISU College of Pharmacy. He earned his PharmD from ISU and completed a clinical pharmacy residency in drug information at the Idaho Drug Information Center. He has been a member of the ISU faculty for 19 years and has been involved with experiential education for the past 9 years. His specialty areas include pharmacy-delivered immunizations, medication therapy management, drug information, and nuclear pharmacy.

For 8 years, Cleveland served on the Executive Board for the Idaho Immunization Coalition and held several leadership positions including chair of the executive board. The coalition created a long-term sustainability plan to secure the longevity of their successful vaccination mission in Idaho during his leadership tenure.

Cleveland coordinates the ISU College of Pharmacy's pharmacy-delivered immunization training, health screenings, immunization clinics, and educational sessions. Over the last 3 years, he has worked with numerous community health care partners on statewide vaccination efforts including coordinating drive-through influenza clinics, COVID-19 vaccination clinics, and increasing vaccination rates in underserved populations in rural Idaho.

Honorable Mention

Uri Bassan, BSPharm

Best Buy Drugs and Rx Innovations, Albuquerque, NM

Uri Bassan, BSPharm, graduated from the University of New Mexico College of Pharmacy in 1998 with a bachelor of science degree in pharmacy. Bassan was already conducting large pop-up vaccination clinics before the pandemic and used that experience to bring the COVID-19 vaccine to rural New Mexico. His efforts were so successful that the *New York Times* featured a story about the program on Thanksgiving Day in 2021.

In 2022, Bassan transformed a New Mexico immunization program that began before COVID-19 and grew exponentially during the pandemic to what is now a model program for how to overcome challenges of a diverse and rural population.

Prior to COVID-19, Bassan was a pharmacy manager at a grocery chain and responsible for coordinating their on-site vaccination program. When COVID-19 began, because of his previous relationship with senior cen-

Immunization delivery training available

APhA's Pharmacy-Based Immunization Delivery certificate training program is based on national educational standards for immunization training from the CDC. This practice-based curriculum represents a fusion of science and clinical pharmacy and emphasizes a health care team approach, seeking to foster the implementation of interventions that will promote disease prevention and public health. The purpose of this certificate training program is to prepare pharmacists with comprehensive knowledge, skills, and resources necessary to provide immunization services to patients across the life span.

More information is available at pharmacist.com/Education/Certificate-Training-Programs/Immunization

ters, assisted living centers, and nursing homes, he was contacted by the New Mexico Department of Aging, a state program, to partner with and to support and scale COVID-19 vaccine administration in the northern part of New Mexico. With his team, he set up vaccination clinics at senior centers, churches, and businesses all over the state, traveling to more than 100 cities and towns.

By the end of 2021, the grocery store chain no longer wanted to support the vaccine program, but the demand for vaccines was higher than ever. Bassan thus start his own business. Working with a local, well-established independent pharmacy (Best Buy Drugs), Uri has taken vaccinating the state of New Mexico to a whole new level. His team of more than 100 employees including pharmacists, pharmacy technicians, medics, physicians, and nurses covers half the state of New Mexico by going to schools, churches, senior centers, assisted living facilities, and other places in the community where people need vaccines.

Corporation/Institution

Focusing on wellness, prevention, and the creation of systems of care, the winners in this category have facilitated the development of practice models supporting pharmacists' immunization roles.

National Winner

Cub Pharmacies' Clinical Programs Team

Cub Pharmacy's established relationship with state and local public health departments became critical as the COVID-19 pandemic hit, and they continued to partner with the Minnesota Department of Health (MDH) and Hennepin County Public Health to expand and support access to vaccinations. Cub Pharmacies is dedicated to vaccinating the underserved, and often marginalized, members of the communities.

Cub Pharmacies cohosted several mass vaccination events with Hennepin County at local public libraries. The events were open to all regardless of insurance status. Cub Pharmacies collaborated with a local nonprofit, Encouraging Leaders, which supports projects that focus on Black, Indigenous, and People of Color youth residing in the poorest neighborhoods in Minneapolis and around the Twin Cities, particularly in neighborhoods with a high crime rate. Cub Pharmacies held multiple events at Encouraging Leaders headquarters, offering hundreds of participants an opportunity to get vaccinated against COVID-19, flu, and receive other routine immunizations.

These successful partnerships and Cub Pharmacies' ability to provide a respectful and seamless experience for participants ultimately lead to a partnership with UCare, a nonprofit health plan company which enabled the establishment of another six underserved vaccination clinic partnerships.

Cub Pharmacies' efforts were recognized at a state level by both the MDH and the Minnesota governor's office. In an introductory email between the MDH and a county public health coordinator, MDH stated "Cub played a pivotal role in the early vaccination of teachers last winter and they've been very active in our mission of health equity in the response."

Honorable Mention

Stanford Health Care IBD Clinical Pharmacy Team

San Francisco, CA

The Stanford Health Care (SHC) Inflammatory Bowel Disease (IBD) Clinical Pharmacy Program was established in 2018. Initially, one pharmacist worked alongside two IBD providers (doctors and physician assistants) during their patient visits, discussing new medications and vaccine recommendations based on current health maintenance guidelines for IBD patients who have increased risk of infection due to their condition.

Only 52% of gastroenterologists get an accurate vaccination history from their patients, and primary care physicians are often unaware of the additional vaccination recommendations involved in treating IBD. This leaves a significant gap in providing necessary vaccinations. The most common infections that lead to hospitalization of patients with IBD are vaccine-preventable, such as pneumonia and shingles.

After a short time of working in clinics, the SHC IBD Clinical Pharmacy Team aimed to provide all of their patients with IBD knowledge of the recommended vaccines and access to

obtain them. After creating approved vaccination guidelines for patients and a Pharmacist Collaborative Practice Agreement (CPA), SHC adjusted their care model to provide a health maintenance consultation to all new patients and opened services to all IBD providers and their patients on a referral basis to reach existing patients in need of vaccination consultation.

SHC's IBD program has five clinic locations throughout the San Francisco Bay Area, composed of a multidisciplinary team of nine IBD prescribers who see approximately 3,500 patients per year.

Pharmacy Team Member

This award recognizes individuals who are not pharmacists but have advocated for immunization efforts and pharmacist-delivered immunizations, including pharmacy technicians, store managers, or other support staff. During the COVID-19 pandemic, these individuals were even more critical to providing care to our communities, and we thank each of them for their collaboration, commitment, and support.

National Winner

Amber Coleman, CPhT

Walgreens

Amber Coleman, CPhT, started as a pharmacy technician in 2004 with Price Chopper in the Kansas City Metro Area. In 2012, after moving to the Gulf Coast area, Amber continued her passion of working in the pharmaceutical area with Kessler Air Force Base before accepting a position with Walgreens in 2014.

Throughout the COVID-19 pandemic and continuing flu seasons, Amber has provided endless support to Walgreens pharmacies in the state of Mississippi. Starting in March 2021, Walgreens received their first doses of the COVID-19 vaccine, and Amber sprang into action by providing support to the community as well as to pharmacists. Her work was critical in setting up and coordinating vaccine administration to long-term care facilities within the state. She was able to set up clinic dates, initiate clinic agreements, procure vaccines, and coordinate with pharmacists to help them administer the COVID-19 vaccines in an efficient and safe manner.

Alongside her role in provided the COVID-19 vaccine, Amber also helps schedule and complete yearly flu vaccine clinics. These flu clinics protect patients in long-term care facilities, local schools, and local businesses. Since starting her role as vaccine, she has helped and supported the protection of over 5,000 patients from COVID-19 and the flu.

Amber has received the Walgreens Champion of Champions Award, Pharmacy Technician Certification Board (PTCB) Educator for the Mississippi District, and 2022 Pharmacy Technician of the Year Award from the Minnesota Pharmacists Association.

Honorable Mention

David (Nate) Ryder, CPhT

Walgreens

David (Nate) Ryder, CPhT, has been a team member at Walgreens since February 2022. He quickly became PTCB-certified and an immunizer

Ryder approached his immunizing role seriously and helped promote many COVID-19 shots with each flu shot he administered. For example, Ryder helped organize a clinic at Ramsey Solutions and assisted the pharmacist in immunizing the entire staff of 200 in 1 day. The pharmacy has currently immunized close to 3,300 patients for COVID-19 since March 2022 and exceeded their goal for flu shots in early November 2022.

Ryder's confidence and congenial bedside manner in the patient room have often brought back patients asking specifically for him. Walgreens' pharmacists can confidently perform their other daily tasks knowing that Ryder has immunizations locked down.

Travel health

National Winner

Beverly Schaefer, BSPharm

Katterman's Sand Point Pharmacy, Seattle, WA

Beverly Schaefer, BSPharm, was named one of APhA's Next Ten Women in Pharmacy, which prompted her staff to create a "Vaccine Queen" window display highlighting many of Beverly's awards.

Katterman's Pharmacy offers a complete line of travel immunizations and medications for travelers of all ages, including infants, and educates people about vaccines that would be most appropriate for their travel needs. Many Seattle businesses and organizations refer travel appointments to Katterman's, making it an immunization champion year round, providing about 15,000 immunizations annually.

Special recognition

Mitchel C. Rothholz, BSPharm, MBA, former APhA Chief of Governance & State Affiliates and Executive Director, APhA Foundation, was recognized for his many years of support for the APhA Immunization Champion Awards.

For nearly 3 decades, Rothholz has been responsible for coordination of APhA's strategic plan, governance and policy development activities, and public health initiatives. As a leader in both the immunization and pharmacy professions, Rothholz has been nationally recognized as an expert on pharmacy-based immunization delivery and as an advocate for the profession of pharmacy on numerous issues.

To download the 2023 Immunization Champion Awards program and view awardee videos, visit the APhA Immunization Resource Center at www.pharmacist.com/immunization-center. ■

Survey finds employers are not meeting pharmacists' expectations for rewards and recognition

Olivia C. Welter, PharmD

Despite pharmacy professionals having more clinical education and opportunities for specialization than ever before, job satisfaction for pharmacists remains low.

Over the years, the American College of Clinical Pharmacy (ACCP) has published several iterations of a white paper describing what motivates pharmacists in their jobs, challenges in achieving success at work, and how opportunities for professional rewards and advancement can be beneficial. The first paper was published in 1995, followed by an update in 2010. The latest edition, titled "Rewards, recognition, and advancement for clinical pharmacists," was published in the *Journal of the American College of Clinical Pharmacy (JACCP)* in March 2023.

Pharmacists ranked financial incentives as their preferred workplace reward with 51% of respondents selecting this option.

What do pharmacists need to improve job satisfaction?

Survey results revealed which factors were most important for pharmacists in their careers. Categories included financial incentives, personal/professional commitment changes, professional advancement, workplace improvement, and employee appreciation.

Pharmacists ranked financial incentives as their preferred workplace reward with 51% of respondents selecting this option. Financial incentives include raises, bonuses, travel funding, and reimbursement for credentials/certifications.

The next-highest preferred reward was personal/professional commitment changes. This category encompassed shift scheduling, autonomy, work flexibility, work-life balance, and staffing support.

While the lowest-ranked reward category was employee appreciation, over 70% of respondents said that some type of recognition by their employer was important to them. Pharmacists preferred public recognition over private recognition.

Contrary to the strong desire of pharmacists to receive financial rewards, only 22% and 20% of respondents said that raises and bonuses are available to them, respectively. Pharmacists also revealed that shift scheduling based on employee preference and additional staffing were lacking at their institutions. Alarmingly, just 17% of respondents said that their employer is committed to work-life balance.

White paper background

The paper was written using data from a web-based survey conducted by ACCP and distributed to ACCP members in March 2022. Primary target participants for the survey included hospital, health-system, and community pharmacists as well as faculty at colleges/schools of pharmacy who had a clinical practice site. The format of survey questions varied, with some using 5-point Likert scales, some requesting ranking of options, some with multiple choices to select from, and opportunities for written responses.

Five hundred and seventy-one pharmacists submitted responses to the survey. Most respondents were 35–49 years old and had been in practice for 5–15 years. Nearly 99% of respondents had completed postgraduate training or held a professional certification of some kind, including 74% who completed PGY-1 residency training, 49% who completed PGY-2 residency training, and 87% who obtained board certification.

Pharmacists who worked at academic medical centers were most well represented in terms of practice setting for participants, followed by Veterans Affairs hospitals, community teaching and non-teaching hospitals, and ambulatory care settings. There were only four respondents who identified as community pharmacists.

ACCP recommendations for rewards, recognition, and advancement

The ACCP Clinical Practice Affairs Committee offered recommendations to health systems and pharmacy administrators for rewards, recognition, and advancement for pharmacists beginning with encouraging employers to evaluate their current systems and where there could be areas for improvement. Other recommendations included

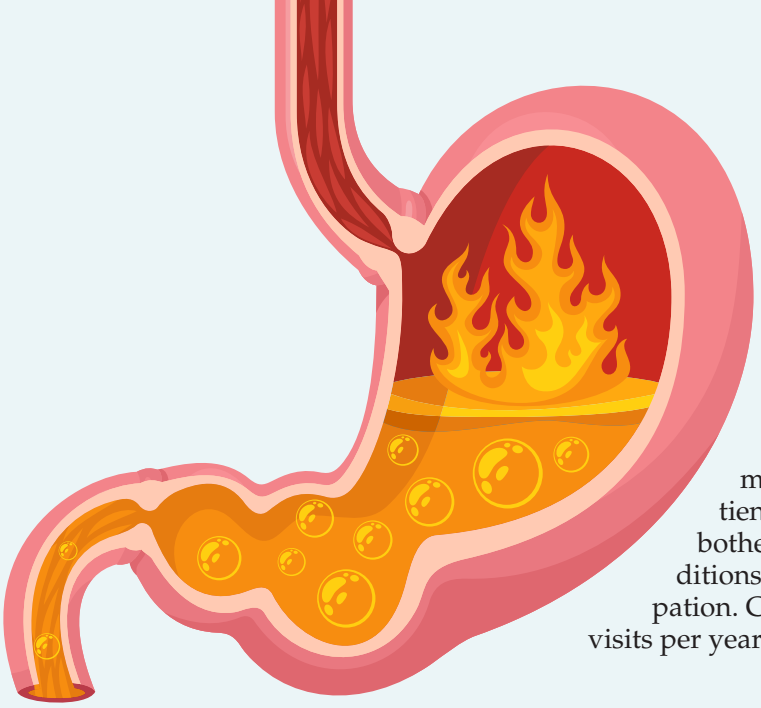
- Prioritizing financial incentives for advanced credential maintenance
- Improving shift scheduling to correlate with employee preferences
- Increasing pharmacist autonomy
- Increasing public/peer recognition of employees, including equity of recognition among pharmacists within the department and between various professions of the institution
- Implementing clear career ladders or personalized professional recognition programs, including separate ladders for clinical and managerial advancement

Professional burnout and well-being

The information highlighted in this white paper helps to explain how employers can improve pharmacists' pride in their career and satisfaction with their positions.

While the survey didn't expressly address pharmacist burnout and well-being, the authors did note in their discussion that potential for burnout and job dissatisfaction will continue to persist if employers do not address pharmacists' needs.

Pharmacists, pharmacy technicians, and student pharmacists can track their well-being using the APhA Well-Being Index for Pharmacy Personnel available at apha.us/APhAWBI to learn more. ■



Gastrointestinal distress

Common GI complaints that can generally be managed with nonprescription treatments and self-care include belching, heartburn, indigestion, acid reflux, sour stomach, and nausea. Nausea accounts for 324,000 emergency department visits for patients aged 65 years and older. Patients also seek quick relief from other common and bothersome intestinal and bowel symptoms and conditions such as bloating, flatulence, diarrhea, and constipation. Constipation leads to at least 2.5 million physician visits per year in the United States.

Gastrointestinal distress

Lactose digestive aid (n = 585)

Lactaid	67%
Schiff Digestive Advantage	1%
Walgreens	1%
Equate	1%
Kirkland	1%

Diarrhea relief (n = 618)

Imodium	66%
Pepto Bismol	9%
Kaopectate	1%
CVS Health	1%
Equate	1%

Gas relief (n = 572)

Gas-X	61%
Mylicon	7%
Phazyme	2%
Gasex	2%
Beano	1%

Hemorrhoid relief (n = 571)

Preparation H	61%
Tucks	7%
Anusol	3%
CVS Health	1%
Walgreens	1%

Upset stomach relief (n = 564)

Pepto Bismol	52%
Tums	10%
Pepcid Complete	4%
Maalox	3%
Emetrol	3%

Fiber supplement (n = 629)

Metamucil	48%
Benefiber	12%
FiberCon	6%
Fiber One	2%
Citrucel	1%

Stool softener (n = 545)

Colace	48%
Dulcolax	12%
Walgreens	2%
CVS Health	2%
Senna-S	2%

Heartburn relief (n = 575)

Tums	35%
Pepcid	18%
Prilosec OTC	8%
Nexium	4%
Mylanta	3%

Laxative (n = 560)

MiraLAX	25%
Dulcolax	23%
Senokot	7%
Colace	6%
Ex-Lax	3%

Nausea treatment/Relief (n = 591)

Dramamine-N	20%
Emetrol	19%
Pepto Bismol	10%
Bonine	4%
Nauzene	3%

Self-care survey redux

This section of *Pharmacy Today*'s Self-Care Product Survey is reprinted from the full survey results published in the January 2023 issue of the magazine and available online at pharmacytoday.org.

The current survey was conducted using scientifically valid methodology and determines those nonprescription products most often recommended by pharmacists in the United States to consumers.

The winners were selected based on a survey of 1,682 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.

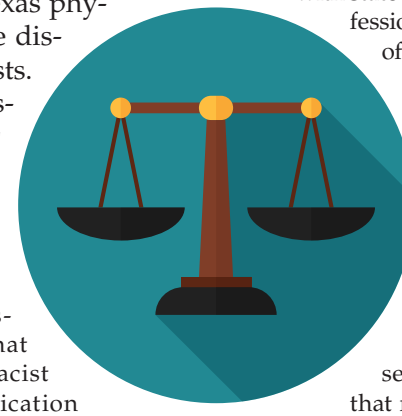
The n value given for each category represents the total number of responding pharmacists' recommendations.

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.

Texas prescriber dispensing restriction upheld by court

David B. Brushwood, BSPharm, JD

The Federal Food Drug & Cosmetic Act determines the classification of pharmaceutical products as being available by prescription only (RxOnly) or OTC. States have the authority to decide who may prescribe and who may dispense RxOnly drugs. Two Texas physicians recently challenged a state law that limits the dispensing of RxOnly medications to licensed pharmacists. The two physicians sued to establish their right to dispense noncontrolled substance medications to their own patients.



Background

Texas law recognizes three exceptions under which physicians are allowed to dispense medications to their own patients: A 3-day supply of medication that is necessary to meet the patient's immediate needs, medication samples provided to the physician free of charge, and physicians practicing in narrowly defined rural areas.

The physicians sued the board of pharmacy and the board of medicine, contending that their right to "pursue a chosen business" recognized under the state constitution was being violated by the state law. They also contended that their state constitutional right to equal protection under the law was being violated. They argued that there is no rational basis for the exception that applies only to rural physicians.

The defendants moved the court to dismiss the lawsuit, and this motion to dismiss was granted. The physicians appealed.

Rationale

The appellate court first addressed the physicians' claim that the state law conflicts with their constitutional right to pursue a chosen business. The physicians contended that the law is unconstitutional because it is not rationally related to a legitimate government interest.

The court disagreed, ruling that "having a pharmacist doublecheck medication before dispensing would correct potential errors and improve the health and safety of patients." The court cited prior case law as well as the 1980 *Sesame Street* episode "Two Heads Are Better Than One."

The court referred to a survey that reported "64% of respondents strongly agreed that 'having a physician/NP and pharmacist both check my medication makes it safer for me to take this medication.'"

The court concluded that the Texas law is not "so burdensome as to be oppressive" regarding the physicians' business interests.

Turning to the physicians' equal protection argument, the court said, "that a narrow exception exists for a handful of rural doctors does not negate the state's previously discussed purpose of ensuring the safe dispensing of medication; rather, it merely reflects the state's attempt to balance that interest with its separate (but related) interest in promoting access to medications for persons who live in rural areas that would otherwise have no or limited access to pharmacies."

The appellate court affirmed dismissal of the case.

The court cited prior case law as well as the 1980 *Sesame Street* episode "Two Heads Are Better Than One."

Takeways

This case illustrates the overlap of federal laws that regulate drug products with state laws that regulate professional practice. The goal of both is to promote the health and safety of patients.

The court ruling upholding the challenged Texas law can be justified based on recognition that pharmacists promote patient health and safety in several important ways that may not be applicable to dispensing prescribers. These include

- Comprehensive review of complete patient medication records, facilitated by computer alerts to identify potential problems with a patient's entire drug regimen
- Established relationships with suppliers who support pharmacists in assuring authentic product provenance and access to trustworthy alternative products during times of drug shortage
- Experience with insurance claims submission and the resolution of obstacles such as a prior authorization requirement
- A standard of practice that includes a pharmacist's final check of every prescription prior to its delivery to the patient

The language of the court recognizes two important pharmacist responsibilities. The first of these is the correction of prescribing errors, and the second is the improvement of patient health and safety. It is necessary but not sufficient for a pharmacist to identify errors in a prescription. To justify their exclusive dispensing role, pharmacists must also promote positive therapeutic outcomes for all patients. ■

Applying layered learning to advance pharmacy practice

Brittany Botescu, PharmD; Paria Sanaty Zadeh, PharmD; and Bella Blankenship, PharmD

The layered learning practice model (LLPM) allows new practitioner pharmacists to precept students and other learners while also being precepted by more experienced practitioners. This is mutually beneficial because it facilitates professional development among learners and preceptors and maximizes benefits to the organization.

The LLPM is championed in a variety of pharmacy practice settings, with numerous examples within the profession. Layered learning can entail collaborations spanning departments and shared experiences across an organization, including at APhA.

Precepting within layers

Brittany Botescu, PharmD, as a recent APhA executive resident, is at the center of layered learning opportunities. After supporting APhA's policy process throughout residency, she now ushers residents through those same responsibilities as APhA senior manager of governance and policy. Botescu channels prior experiences to guide resident activities, such as developing policy background materials and facilitating committee meetings. She also engages learners in discussions on the broader aspects of policy development.

"Reflecting on mentors in my career, they not only impart their knowledge to new practitioners, but also embody continuous professional development. To me, layered learning means building upon my previous experiences while empowering others to do the same," said Botescu.

(From left) Paria Sanaty Zadeh, Brittany Botescu, and Bella Blankenship engage in layered learning through their work at APhA.

Bella Blankenship, PharmD, is in the same executive resident role as Botescu was previously. "As a recent graduate and current association management resident, I have seen firsthand how layered learning positively contributes to the professional growth of everyone involved," said Blankenship. "There is much to be gained from combining perspectives across a diversity of backgrounds and experience levels. Taking part in layered learning has shaped my viewpoints on a vast array of issues impacting our profession."

During APhA's 2022–2023 policy cycle, Botescu precepted Blankenship to prepare a comprehensive policy paper and lead policy discussions with members. Blankenship's residency experience presents opportunities for her to participate in the LLPM with her preceptors and APPE students. As student pharmacists rotate through the association, Blankenship guides them on APhA's practice and advocacy priorities while deepening her work in these areas.

A shared element between Blankenship's and Botescu's experiences is the precepting and mentorship received from the APhA practice and professional affairs team, which includes Paria Sanaty Zadeh, PharmD, associate director of practice and science programs. Sanaty Zadeh serves as a subject matter expert in the annual policy process, reviewing APhA executive residents' policy projects and providing input on proposed policy statements. She precepts residents before, during, and after Academy policy committee meetings, delegate caucuses, and APhA House of Delegates sessions. To foster in-depth precepting experiences, she integrates real-world insights from her work in varied pharmacy settings.

"I frequently draw on prior experiences from practicing and precepting in an academic medical center with various learners. I'm thrilled to continue incorporating layered learning and offering a dynamic learning experience in my role at APhA. Seeing the teaching and learning process unfold together is energizing and provides an enriched team-based experience," said Sanaty Zadeh.

Takeaway

Layered learning is not unique to associations. Similar opportunities are possible in all traditional and nontraditional pharmacy practice settings. ■

Tips for success with layered learning

Postgraduate preceptors	New practitioner preceptors	Experienced preceptors
1. Reflect on past learning experiences. What preceptor skills facilitated a positive experience?	1. Reflect on past preceptors whom you would like to embody. What made them effective?	1. Reflect on previous precepting experiences. What methods helped you succeed?
2. Ensure your precepting role is clearly delineated in the layered learning arrangement.	2. Understand your role as a learner and preceptor. Approach both with humility and curiosity.	2. Advise newer preceptors on balancing their precepting role with other responsibilities.
3. Seek constructive feedback early in your career to hone your skills.	3. Be receptive to feedback as a newer preceptor, and offer thoughtful feedback to others.	3. Establish bidirectional feedback with all learners. Incorporate suggestions into future learning experiences.
4. Learn from past successes and opportunities for continuous improvement.	4. Embrace the continuous nature of learning. Be attentive, patient, and adaptable to change.	4. Encourage strategies for continuous improvement for all, including yourself.

Inpatient*Insights*

Antibiotics prevalent in nursing homes

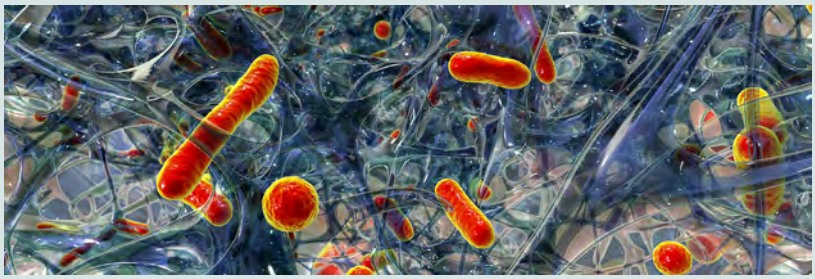
While promoting antibiotic stewardship is important to the health of all patients, overprescribing of antibiotics is a particular problem among nursing home patients. According to a recent paper published on April 5, 2023, in the *Journal of Infectious Diseases*, antibiotics are among the most frequently prescribed medications in nursing homes, and up to 85% of prescribed antibiotics are inappropriate or unnecessary.

Nursing home residents are particularly vulnerable to adverse outcomes from antibiotic use, such as *Clostridioides difficile* infection, which not only affects residents who are prescribed antibiotics, but can be transmitted to other residents in the facility.

Researchers at the Brown University School of Public Health studied a national cohort of older adults residing long-term in U.S. nursing homes between 2013 and 2017 and calculated period prevalence estimates for antibiotic prescribing, rates of prescribing, and days of therapy. They found that among 1,375,062 residents, 66.2% were prescribed at least one antibiotic during the nursing home stay. The median number of antibiotic courses per resident was two and overall, residents received 41.6 days of antibiotic treatment per 1,000 days of care.

The most prevalent antibiotic classes were fluoroquinolones, sulfonamides and related agents, and first-generation cephalosporin. Sulfamethoxazole-trimethoprim, levofloxacin, and ciprofloxacin were the most prevalent antibiotics.

The authors suggest that their results can inform antibiotic stewardship interventions to reduce antibiotic overprescribing, improve appropriateness, and reduce related adverse outcomes in nursing homes. ■



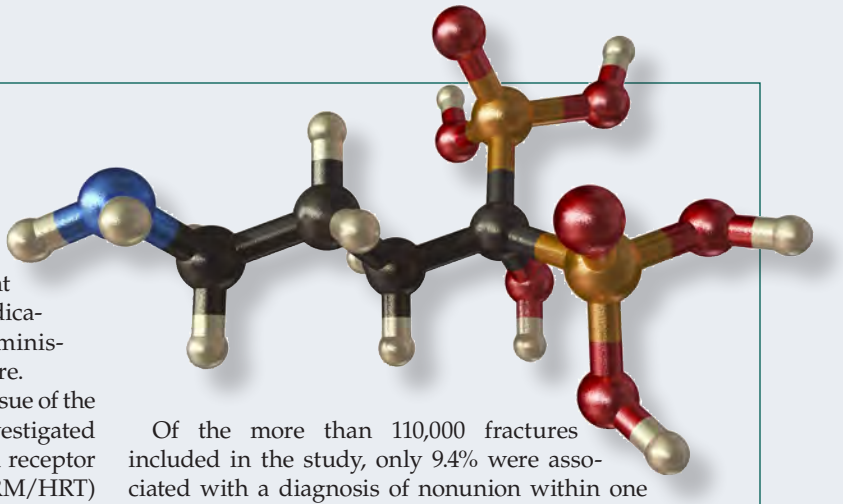
Comparing the efficacy of antibiotics for spontaneous bacterial peritonitis

For patients with liver cirrhosis, spontaneous bacterial peritonitis (SBP) is one of the most serious complications of the disease. Initial treatment consists of the use of antibiotics, including cefotaxime, ceftriaxone, and ciprofloxacin. Increasing antibiotic resistance, however, has led researchers to question if the three antibiotics are comparable and still appropriate for clinical treatment of SBP. A recent study, published in the April 2023 issue of the *American Journal of Gastroenterology*, compared the current efficacy of cefotaxime, ceftriaxone, and ciprofloxacin for the treatment of SBP in patients with cirrhosis with ascites.

Researchers from eight universities in Korea conducted a multicenter, prospective, randomized controlled trial that included 261 patients with liver cirrhosis with ascites randomized to receive one of the three subject antibiotics.

A follow up paracentesis was performed after 48 hours of treatment to allow a change of antibiotic in the absence of an initial response, defined as a >25% decline in polymorphonuclear cell count. Further evaluations were done after 120 hours (the primary endpoint) and 168 hours of treatment.

Resolution rates at the primary endpoint were 67.8%, 77.0%, and 73.6% in the cefotaxime, ceftriaxone, and ciprofloxacin groups, respectively, and the 1-month mortality was similar among the groups. The authors concluded that the efficacy of the three antibiotics was not significantly different when using response-guided therapy and that they are still efficacious as the initial treatment for SBP, especially in patients with community-acquired infections. ■



Bisphosphonate use OK after long-bone fractures

Fragility fractures among older patients often necessitate initiation of osteoporosis treatment. While the use of bisphosphonates is the current standard of care for medical management of osteoporosis, it's unclear if osteoporosis medications increase the risk of nonunion when administered after surgical treatment of an acute fracture.

In a recent study published in the April 2023 issue of the *Journal of Bone and Joint Surgery*, researchers investigated whether bisphosphonates or selective estrogen receptor modulators/hormone replacement therapy (SERM/HRT) are associated with nonunion following fracture in a population of older adults.

The authors conducted a retrospective analysis of Medicare claims from 2016 to 2019 to identify patients more than 65 years old who had a surgically treated long-bone fracture and successive claims were linked for each beneficiary through one year following the fracture to determine fracture union status. Multivariable logistic regression models were specified to identify the association between medications and fracture union status while controlling for age, sex, race, Charlson Comorbidity Index (CCI), and fracture type.

Of the more than 110,000 fractures included in the study, only 9.4% were associated with a diagnosis of nonunion within one year. Bisphosphonate use was more common in the nonunion group (12.2% vs. 11.4%), but when controlling for race, age, sex, and CCI, neither bisphosphonates nor SERM/HRT were associated with nonunion. Bisphosphonate use within 90 days post-fracture was not significantly associated with nonunion and the timing of medication administration did not influence fracture union status.

The authors concluded that orthopedic surgeons should not withhold or delay initiation of bisphosphonate or SERM/HRT for osteoporosis after acute fracture out of concern for nonunion. ■

LDC medications effective for initial management of hypertension

Low-dose combination (LDC) medications consisting of three or four antihypertensive drugs have emerged as a potentially important therapy for the initial management of hypertension. Researchers at the University of New South Wales, Royal Prince Alfred Hospital, the University of Sydney, Northwestern University, Washington University in St. Louis, and the University of Kelaniya (Sri Lanka) conducted a systematic review and meta-analysis of seven trials enrolling 1,918 patients and found that LDC antihypertensives were more efficacious than monotherapy, usual care, or placebo in terms of mean BP reduction and achieving a BP target. Four trials involved triple-component LDC and four involved quadruple-component LDC.

The researchers found that at 4 to 12 weeks' follow up, LDC medications were associated with a greater mean reduction in systolic BP than initial monotherapy, usual care, and placebo. LDC medications were also associated with a higher proportion of participants achieving BP <140/90 mm Hg at 4 to 12 weeks compared to monotherapy, usual care, and placebo.

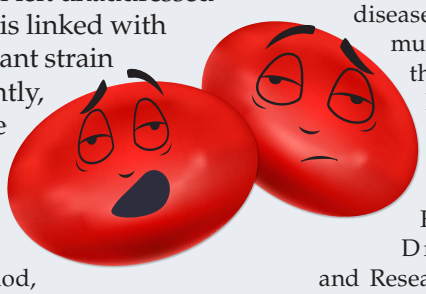
They found no significant heterogeneity between trials enrolling patients with and without baseline BP-lowering therapy. Results from two trials indicated that LDC medications remained superior to monotherapy or usual care at 6 to 12 months. LDC medications were associated with more dizziness but no other adverse effects nor treatment withdrawal.

The authors concluded that the study, published on April 26, 2023, in *JAMA Cardiology*, showed evidence that LDC medications may be an effective strategy for the early management of hypertension. ■

First oral agent approved for anemia in patients with CKD receiving dialysis

Corey Diamond, PharmD

Chronic kidney disease (CKD) is a growing health issue worldwide that impacts approximately 700 million individuals, with nearly 14% of patients with CKD also experiencing anemia. If left unaddressed or not properly treated, anemia resulting from CKD is linked with unfavorable clinical outcomes and imposes a significant strain on both patients and health care systems. Until recently, there has been a need for new oral therapies that are equally as effective and safe as existing treatments.



On February 1, 2023, FDA announced the approval of daprodustat (Jesduvroq—GSK) as the first treatment for anemia in end-stage renal disease that can be taken via the oral route. The medication is currently the only one approved for use in patients who have been receiving dialysis for at least 4 months.

ASCEND-D

The approval of daprodustat was based on the results of the Phase 3 ASCEND-D trial—published by Singh and colleagues in *NEJM* in November 2021—which included over 2,900 patients with end-stage renal disease on dialysis with anemia. The trial was a randomized, open-label, active-controlled, parallel-group, event-driven study conducted at 431 centers in 35 countries. Participants were randomized to either receive daprodustat or recombinant human erythropoietin (rhEPO) plus a placebo.

The study's two primary endpoints were time to first occurrence of a major adverse cardiovascular event (i.e., a composite of death from any cause, nonfatal myocardial infarction, or nonfatal stroke) and the mean change from baseline in hemoglobin levels during the pre-defined evaluation period.

The results of ASCEND-D demonstrated that dialysis patients taking daprodustat had a mean change in hemoglobin of 0.3 g/dL compared to 0.1 g/dL in the rhEPO group, which achieved the goal noninferiority margin of –0.75 g/dL. Additionally, during the 2.5-year major adverse cardiovascular event (MACE) follow-up period, dialysis patients who received daprodustat experienced a MACE event rate of 25.2% versus 26.7% in patients receiving rhEPO, achieving the goal noninferiority margin of 1.25.

Key differences

Patients in end-stage renal disease almost always progress to a state of chronic anemia due to a reduction in kidney function that affects their ability to produce a hormone known as erythropoietin, which signals the body to produce red blood cells.

> The medication is currently the only one approved for use in patients who have been receiving dialysis for at least 4 months.

Currently, the only treatments available for this are protein analogs known as erythropoietin stimulating agents (ESAs). However, their design as hormone analogs makes it difficult to formulate an oral option. ESAs are only available via I.V. and S.C. routes.

Daprodustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI). HIF-PHIs inhibit oxygen-sensing prolyl hydroxylase enzymes which, in turn, stabilizes hypoxia-inducible factors. This process mimics the mechanism in the human body at high altitudes and is theorized to increase the transcription of erythropoietin in the kidneys. Its chemical structure also allows it to be delivered, conveniently, through the oral route.

"With an oral drug option in addition to the FDA-approved injection options, adults with chronic kidney disease on dialysis now have multiple ways to treat their anemia," said Ann Farrell, MD, director of the Division of Non-Malignant Hematology in FDA's Center for Drug Evaluation and Research in an FDA news release. "This approval demonstrates FDA's commitment to helping bring a range of therapeutic options to patients with chronic diseases. Patients can consult with their health care providers to select the option that is most appropriate."

Safety and warnings

While the mechanism of daprodustat may be novel, the ASCEND-D trial did not provide sufficient evidence to suggest that its adverse effect profile is safer than ESAs.

Similar to ESAs, daprodustat contains a boxed warning for increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access. Additionally, likewise to ESAs, targeting a hemoglobin level >11 g/dL with daprodustat is expected to confer similar risk of death and arterial venous thrombotic events.

No trial has yet to identify a daprodustat dosing strategy that does not increase these risks; thus, the lowest dose of daprodustat should be used to achieve therapy goals. ■

FDA authorizes 503Bs to assist liquid pain reliever shortage

Sonya Collins

As the "triple-demic" of COVID-19, influenza, and respiratory syncytial virus raged through the fall and winter, drug manufacturers found themselves unable to keep up with increased demand for children's liquid ibuprofen and other liquid pain relievers and fever reducers. In response to the shortage, FDA released new guidance in February 2023 outlining how 503B outsourcing facilities could offer some assistance.

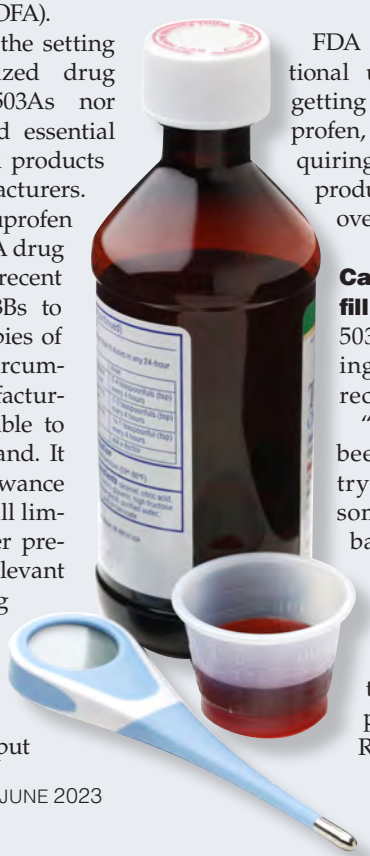
New FDA guidance

The FDA guidance allows for 503B outsourcing facilities to compound liquid ibuprofen to make available for sale to hospitals and health systems for administration within the facility and to state-licensed pharmacies, including those within hospitals and health systems, and applicable federal facilities to dispense for home use to patients who have a valid, patient-specific prescription.

"I think this will play an active role in helping satisfy the shortage," says Lee Rosebush, PharmD, JD, chairman and general counsel, Outsourcing Facility Association (OFA).

By law, outside of the setting of an FDA-recognized drug shortage, neither 503As nor 503Bs can compound essential copies of commercial products made by drug manufacturers. Without adding ibuprofen suspension to the FDA drug shortage list, the recent guidance allows 503Bs to produce essential copies of the drug, in certain circumstances, until manufacturers are once again able to meet consumer demand. It makes no such allowance for 503As, who are still limited to "four or fewer prescriptions for the relevant compounded drug product in a calendar month."

"It would have been more valuable for FDA to officially put ibuprofen on the shortage list so that 503A pharmacies could help patients in their local communities," says Matt Martin, PharmD, coordinator-elect for APhA's Compounding Special Interest Group.



FDA has added an additional unnecessary barrier to getting the compounded ibuprofen, Martin added, by requiring a prescription for a product that is usually sold over-the-counter.

Can 503Bs alone fill the gaps?

503Bs are currently making several drugs in FDA-recognized shortages.

"The idea that we've been able as an industry to pivot and make some of these shortage-based drugs is an eye opener for those on the Hill, as well as at FDA, to say look, we have an industry here who makes products domestically," Rosebush said.

Critics of the FDA guidance question whether the plan is sufficient to meet what they see as an urgent need and cite many flaws in the plan.

First, 503As do not know which 503Bs are compounding ibuprofen, and 503Bs do not know which 503As would be willing to buy from them. There isn't an existing market for the two entities to do business with each other in this way. As of March 7, 2023, the last time OFA's list was updated, one OFA member organization was offering liquid ibuprofen, according to Martin.

Furthermore, Martin said, buying from them could conflict with wholesale regulations. Section 503B of the Food Drug and Cosmetic Act prohibits 503Bs from wholesaling and requires "not for resale" labels on every product.

> "It would have been more valuable for FDA to officially put ibuprofen on the shortage list so that 503A pharmacies could help patients in their local communities."

"Many pharmacists would regard the sale of the compounded drug product by a 503B outsourcing facility to a 503A pharmacy as an act of wholesaling, and the label on that product would instruct the pharmacy not to resell it to the patient," Martin said. "Boards of pharmacy may also have questions or concerns regarding the interpretation of wholesaling by outsourcing facilities that would need to be addressed."

FDA has stated that it will offer guidance on the wholesale regulation issue, but it has not so far.

Rosebush encourages pharmacists themselves to contact their state boards of pharmacy to ensure they recognize the FDA guidance. "It would be helpful for state boards to recognize that Bs have the ability to do this at the federal level and that way it's more publicly recognized across the industry that this is a possibility for you to get your products." ■

Certain medications may affect ICU readmission risk

Ariel L. Clark, PharmD

Increased patient morbidity and mortality as well as costs to the health care system are seen as a direct result of ICU readmissions after discharge. Despite continual efforts to improve in this arena, there remains a significant portion of patients affected by readmissions. According to a 2016 study in *Critical Care Medicine*, rates for ICU readmissions after discharge were 14.5%.

As researchers have continued to study causation in order to better understand readmission prevention, a recent article published January 25, 2023, in *JAPhA* by Meckel and colleagues attempts to further narrow causes of ICU readmissions by relating them to medications by class—a previously unstudied connection.

Potentially preventable medication-related readmissions accounted for 25% of total readmissions found in this study, 4 additional days in the ICU, and a price tag of over $1 million.

Authors of the study sought to identify which ICU readmissions were a direct result of a medication error, then further determine which classes of medication were most commonly seen in these cases and if a pharmacist intervening could have resulted in fewer ICU admissions.

Identification techniques

The National Coordinating Council for Medication Error and Prevention defines a medication error as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer."

Similar to in outpatient pharmacies, there are several different types of medication errors that can occur within the hospital setting, including omission, commission, administering, and prescribing.

Nonmodifiable patient risk factors, like sex, weight, severity of illness, and others, have been studied successfully for years. Meckel and colleagues noted that the same scoring systems that use these factors to predict risk for overall morbidity and mortality can also be used to assess patient risk for readmission, including the Badawi and Braslow readmission and mortality tools and the Stability and Workload Index for Transfer.

However, while accurate, these predictive tools do not take into account which medications patients do or do not receive upon discharge, which the investigators noted is an error "given that one medication error occurs for every five doses of medications administered in the ICU."

Pharmacists play a critical role in helping prevent medication errors, especially as their roles have expanded.

Impact of pharmacists

Pharmacists play a critical role in helping prevent medication errors, especially as their roles have expanded.

As far back as 2013, researchers, including Leape and colleagues in their *Hospital Pharmacist* paper, have noted that pharmacist staffing in the ICU reduced preventable medication errors. Similarly, in this 2023 study, Meckel and colleagues found that of the PPMIRs, 67.4% occurred when there was not a pharmacist rounding with the other unit staff.

Medication culprits

The Institute for Safe Medication Practice (ISMP) categorizes medications as "High Alert" if the consequences of their use in error will cause significant patient harm. Meckel and colleagues found four of the most commonly seen medications in PPMIRs are what ISMP considers "High Alert" medications. These high-alert medications include anti-infectives, opioids, benzodiazepines, and antiarrhythmics as well as diuretics, which might be most surprising to clinicians.

Study investigators noted that fluid balance is a notoriously tricky task in hospitalized, critically ill patients. However, of the 14 cases analyzed in the study period in which a patient was readmitted to the ICU due to a fluid imbalance, authors noted that initiating or continuing a diuretic could have prevented 13 readmissions.

The authors noted that the results of this study showcase how, as roles continue to expand, pharmacist involvement can improve patients' safety and deter costly ICU readmissions. ■

A minute with ...

Sarah Vas, 2024 PharmD candidate

Purdue University College of Pharmacy, West Lafayette, IN

Member since 2019

"Being a member of APhA–ASP has provided me countless invaluable experiences as a student pharmacist. These experiences have expanded my leadership skills, increased my confidence as a future provider, and empowered me to push the boundaries. APhA–ASP has given me the freedom to challenge myself, while supporting me every step of the way."

How has APhA helped you establish meaningful connections?

APhA has helped me establish meaningful connections through both local and national events. The abundance of opportunities connecting students and pharmacists together has allowed me to expand my network on a vast scale. I have benefited from collaborating with local chapters within Indiana as well as attending the APhA's Annual Meeting & Exposition this past spring. Being the largest pharmacy organization, APhA has introduced me to amazing individuals within the pharmacy profession who I hope to cross paths with over the years.

How has APhA helped prepare you for your career as a pharmacist (e.g., experiences in patient care projects, leadership opportunities, advocacy, etc.)?

The vast leadership opportunities within APhA–ASP have opened doors for me to grow in preparation for a career in pharmacy. As the current Purdue University chapter president, I have expanded my communication, time-management, and delegation skills. Through APhA, I've found a passion for supporting others on an administrative and logistic scale and hope to apply the knowledge gained over the next year to a future career in clinical pharmacy.

What excites you about the profession of pharmacy?

I am most excited about the change and growth within the profession of pharmacy. Health care professionals are recognizing the important role pharmacists play in properly caring for patients. Our scope of practice is constantly expanding, and pharmacists are valued now more than ever. I am looking forward to joining the effort of providing exceptional, holistic care to patients upon my graduation.

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?

As an intern within the outpatient setting, I work longitudinally with patients to assist and counsel them on proper medication adherence. During these appointments, I guide patients in filling pillboxes, educate them on medication changes, and work to eliminate barriers impacting their care.

One patient in particular recently underwent a liver transplant and was prescribed a complex medication regimen. He was primarily Spanish-speaking and struggled to understand the medication list and bottles. He found himself with a heavy pill burden and a stringent routine, creating a high potential for poor adherence.

The patient was referred to our patient care services, and I was able to set up weekly meetings with him and his caregiver. Over the 5 weeks spent with this patient, I used translation services to create a Spanish medication guide, assisted in enrolling him for a COVID-19 vaccine, and supported him in navigating insurance challenges. Each week, I saw improvements in understanding and confidence as this patient became familiar with his medications and pillbox routine. Eventually, the patient presented with excellent adherence and lab results, indicating proper post-transplant management. ■

SDOH screening tool

Make an IMPACT

As a pharmacist, have you ever considered the impact of social determinants of health (SDOH) on your patients? These are the conditions in which people are born, grow, live, work, and age that have a significant impact on their health and well-being. SDOH includes factors such as socioeconomic status, race, gender, education level, employment status, housing conditions, access to healthy food and safe environments, and social support networks. To provide comprehensive care to our patients, it's essential to consider the whole person and not just their symptoms, medication, and medical history.

As one of the most accessible health care providers, pharmacists can play a vital role in identifying and addressing SDOH in their patients. By screening and assessing patients for SDOH, pharmacists can provide targeted interventions to improve health outcomes and reduce health disparities. APhA recognizes the importance of addressing SDOH and offers a variety of screening resources to help pharmacists identify these factors in their patients. These tools can help assess SDOH related to food insecurity, literacy, and cultural competency.

The next time you're counseling a patient, consider asking about their living conditions, access to healthy food, and social support networks. You might be surprised by what you discover and how you can make a difference. Visit pharmacist.com/sdoh to learn more. ■

Did you know?

Reimbursement for billing primer

Did you know that you may be able to get reimbursed for the clinical services you provide under Medicare's Outpatient Fee-for-Service (FFS) program? If not, don't fret—APhA has got you covered.

The APhA Outpatient Fee-for-Service Billing resource is your go-to guide for understanding the opportunities for payment of clinical services provided by pharmacists. With this resource, you can learn about the various services that are reimbursable under Medicare FFS, such as medication therapy management, immunizations, and chronic care management.

But that's not all. The APhA resource can also help you navigate the complexities of the Medicare billing system. You can learn about the documentation and coding requirements necessary for billing clinical services and stay up to date with changes in Medicare billing rules and regulations.

By utilizing the APhA Outpatient FFS Billing resource, you can improve patient care and generate additional revenue for your pharmacy practice. Take advantage of this valuable resource today and discover the opportunities for payment of clinical services provided by pharmacists under Medicare's Outpatient FFS program. Visit apha.us/BillingCenter to learn more! ■

Did you know?

Transitioning Membership

Student pharmacists who are graduating in 2024 are eligible for APhA's Transitioning Membership! The 24-month membership provides extensive resources to support students entering their rotation year.

The APhA NAPLEX Review Guide, a one-year Subscription to Pyrls, and an APPE Pocket Guide are just a few of the most valued benefits included in this membership. Enrollment started April 1, 2023. The students pictured with special APhA tote bags earned an APhA Surprise Pack for registering for Transitioning Membership early—during APhA2023.

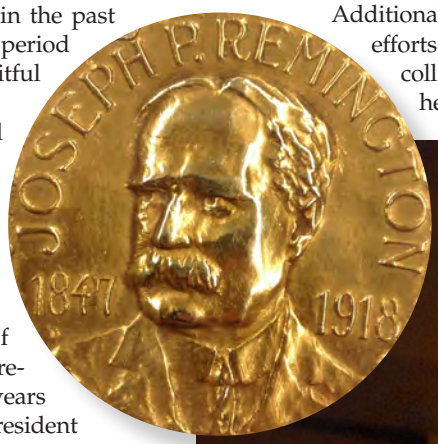
Last call to 2024 graduates! Join APhA's Transitioning Membership before it's too late! Learn more or register at: www.pharmacist.com/transitioning-membership. ■

Honoring leadership, service, and commitment to the advancement of the pharmacy profession

The APhA Awards and Honors Program is the most comprehensive recognition program in the pharmacy profession. Every year at the APhA Annual Meeting & Exposition, pharmacists and other professionals are recognized and honored for their achievements and contributions in the community, the profession, and beyond. Among the many accomplished and deserving professionals honored this year, a few are highlighted below.

The highest honor

Henri R. Manasse, Jr., PhD, ScD (Hon), FFIP, of Downers Grove, IL, is the recipient of the **2023 Remington Honor Medal,** the highest pharmacy honor bestowed by APhA. The award recognizes distinguished service on behalf of American pharmacy during the preceding years, culminating in the past year, or during a long period of outstanding or fruitful achievement.



Manasse has served in many roles throughout his accomplished career and is currently a professor and dean emeritus of the University of Illinois at Chicago, College of Pharmacy. Manasse previously served for 14 years as executive vice president and CEO at the American Society of Health-System Pharmacists following more than 30 years of experience in numerous other positions within academia and public policy. Manasse is a pharmacy graduate of the University of Illinois at the Medical Center. He received his master's degree from Loyola University, and he was the first PhD graduate of the University of Minnesota's Social and Administrative Pharmacy graduate program.

Manasse was selected for this honor due to his extensive service to the profession as a leader who touched many areas of pharmacy practice and education.

Manasse's nominators described his impact on the profession of pharmacy as having been broadly influential in defining an elevated role of pharmacists in society and supporting the advancement of education to fulfill this role. Additionally, Manasse's efforts to educate and collaborate with health care leaders, government officials, and other groups outside of pharmacy have expanded the ability for pharmacists to provide enhanced, collaborative patient care.

Manasse was selected for this honor due to his extensive service to the profession as a leader who touched many areas of pharmacy practice and education.

Nominators also described Manasse as having been at the forefront of pharmacy advancement that included a global impact through leadership positions with the International Pharmaceutical Federation. Lastly, through almost 200 publications or contributions to journals or textbooks he has provided

Henri R. Manasse Jr., PhD, ScD (Hon), FFIP accepts the Remington Honor Medal.

extensive review, analysis, and direction for the profession, which has advanced the profession of pharmacy and its external recognition.

Profession-wide awards

The Hugo H. Schaefer Award, presented to **Ruth A. Smarinsky, PharmD**, of Goleta, CA, recognizes outstanding voluntary contributions to the organization, the profession, and society. Smarinsky is Senior Advisor for Direct Relief, an international humanitarian organization that provides donations of medicines and other health resources to vulnerable people in more than 100 countries. Smarinsky has been actively involved with growing the Direct Relief's programs to increase access to medication at community clinics and health centers throughout the United States, both on an ongoing basis and during times of disaster. She has developed several innovative programs, including a bulk patient assistance program, hurricane preparedness kits, and national distribution of naloxone. Direct Relief has since grown to be the largest charitable organization for the distribution of prescription drugs in the United States. Much of her career has been devoted to providing access to quality pharmaceutical care for underserved patients. She has served as volunteer faculty for the University of California, San Francisco School of Pharmacy (her alma mater), Western University School of Pharmacy, and USC School of Pharmacy.

Remington Honor Medal winners. Top row left to right: Lowell Anderson, DSc, FAPhA, Colonel (Ret) John D. Grabenstein, RPh, PhD, FAPhA, FASHP, Leslie Z. Benet, PharmD, PhD, Peter H. Vlasses, PharmD, BSc (Hon), FCCP, and Paul W. Lofholm, PharmD.
Bottom row left to right: Daniel Hussar, BSPharm, PhD, Marialice Bennett, BSPharm, FAPhA, Henri R. Manasse Jr., PhD, ScD (Hon), FFIP, Lucinda Maine, RPh, PhD, FAPhA, and Harold Godwin, BSPharm, MS, RPh, FAPhA, FASHP.

The **Hubert H. Humphrey Award,** presented to **Farah M. Jalloul, BS, PharmD, MBA,** of Lansing, MI, recognizes APhA members who have made major contributions in government and legislative service at the local, state, or national level. Jalloul was recognized for her contributions as the Director of Professional Development at the Michigan Pharmacists Association. During the COVID-19 pandemic, she transitioned into a liaison role between the MPA and the Michigan Department of Health and Human Services. She facilitated discussions between the state and pharmacists throughout of Michigan and continues to serve as the state's pharmacy emergency preparedness coordinator.

The **Good Government Pharmacist-of-the-Year Award,** presented to **Corrie Sanders, PharmD,** of Honolulu, HI, recognizes an individual pharmacist who contributes to the community through their active involvement in the political process. Sanders was recognized for her contributions serving as president of the Veterans Affairs Pacific Islands Healthcare Systems. ■

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Updates in prostate cancer: What a pharmacist needs to know

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In 2020, approximately 3.3 million men were living with prostate cancer in the United States.[1] Screening recommendations, risk classification, and treatment approaches are constantly evolving, and more than ever before guidelines emphasize shared decision-making and quality of life. It is therefore imperative that pharmacists have the knowledge and tools to help patients navigate screening and treatment choices. Pharmacists are perfectly positioned to discuss the benefits and risks of prevention strategies, review screening recommendations, and present treatment approaches including active surveillance and pharmacologic options.

Incidence and risk factors

Prostate cancer is the second most common type of cancer in the United States, with an estimated 288,300 new cases in 2023, representing 14.7% of all new cancer cases.[1] Approximately 12.9% of men will be diagnosed with prostate cancer at some point during their lifetime.[1] Fortunately, nearly three-fourths of prostate cancer is diagnosed as localized disease, which has an excellent prognosis.[1] The 5-year survival of localized prostate cancer is 100%, compared to 34.1% for patients with distant metastases.[1]

One of the most significant risk factors associated with prostate cancer is older age. The median age of diagnosis is 67 years and people under the age of 40 years are rarely diagnosed with the disease.[1]

Race has also been linked to prostate cancer risk. Compared to non-Hispanic white men, non-Hispanic Black men are more likely to develop prostate cancer (184.2 vs. 111.5 new cases per 100,000 men) and twice as likely to die from prostate cancer (37.5 vs. 17.8 deaths per 100,000 men).[1] These health disparities require further investigation.

Men with a family history of prostate cancer are at increased risk, particularly those with a first-degree relative who was diagnosed at a young age.[2] Germline mutations in DNA repair genes (e.g., *BRCA2*) have also been associated with an increased risk of prostate cancer.[3] Other factors including diet, obesity, and smoking have an unclear association with the risk of developing prostate cancer.

Screening recommendations

Advising patients on prostate cancer screening can be challenging because guidelines are not universally consistent. The authors of each guideline must attempt to weigh the potential harms of screening with the modest overall benefit that has been reported for the general population. Therefore, the goal is to identify patients with high-risk, localized disease who may

Learning objectives

At the completion of this activity, the participant will be able to

- Review the screening recommendations, clinical presentation, and diagnosis of prostate cancer, including the different classifications and stages.
- Identify appropriate pharmacotherapy for patients based on stage of prostate cancer as well as the patient's comorbidities, medications, and goals of care.
- Discuss recent landmark trials and updates to national prostate cancer guidelines.

1. According to the American Cancer Society, a man with a life expectancy of 30 years who has two first-degree relatives who were diagnosed with prostate cancer at a young age should have the opportunity to make an informed prostate cancer screening decision with their health care provider starting at what age?

a. ≥40 years
b. ≥45 years
c. 50–69 years
d. ≥70 years

2. A patient inquires about the potential benefits of selenium and vitamin E for the prevention of prostate cancer. Which of the following most accurately summaries the results of the SELECT trial?

a. More men developed prostate cancer in the placebo arm compared to the selenium arm.
b. Compared to placebo, selenium plus vitamin E significantly reduced the risk of prostate cancer.
c. Compared to placebo, vitamin E significantly increased the risk of prostate cancer.
d. There was no difference in the risk of prostate cancer between all four treatment arms.

3. Xerostomia is a significant adverse effect commonly reported with which prostate cancer therapy?

a. Radium Ra 223 dichloride
b. Lutetium Lu 177 vipivotide tetraxetan
c. Docetaxel
d. Olaparib

be eligible for definitive treatment, ultimately preventing morbidity and mortality associated with advanced disease.

Medical conditions, life expectancy, and patient preferences are vital considerations for screening. Randomized trials in men ages 55–69 years have demonstrated that screening programs prevent approximately 1.3 prostate cancer–related deaths over 13 years per 1,000 men screened.[4,5] Additionally, an estimated three cases of metastatic prostate cancer per 1,000 men screened can be prevented through screening programs.[4]

However, large randomized trials have not demonstrated a reduction in all-cause mortality.

In 2012, the United States Preventive Services Task Force (USPSTF) recommended against routine prostate-specific antigen (PSA)–based screening.[6] As a likely result, PSA-based screening declined in 2013 in comparison with 2010, and a rise in the diagnosis of advanced disease was reported between 2008 and 2014.[6] The USPSTF subsequently updated its recommendation in 2018 to include shared decision-making in men aged 55–69 years.[7] Guidelines from the USPSTF, the American Cancer Society, and the American Urological Association are summarized in Table 1.[7–9] Additional screening recommendations are available through the National Comprehensive Cancer Network (NCCN).[10]

Although the prostate cancer screening guidelines are not uniform in their recommendations, the importance of informed and shared decision-making has been consistently emphasized. Patient education materials have been developed but have been criticized for being too complex. Furthermore, only 29% of patients surveyed reported that a physician informed them PSA testing was a choice.[11] As one of the most trusted health care professionals, pharmacists can play a key role in educating patients on PSA-based screening and the benefits versus harms of early detection.

The primary benefits of early prostate cancer detection and treatment are prevention of metastatic disease and prostate cancer deaths. However, the harms must also be considered. These include adverse effects associated with screening and subsequent harms of diagnosis and treatment.

A false-positive screening may result in unnecessary stress and psychological harm. Unfortunately, false-positive rates in prostate cancer screening are relatively common with one trial reporting a rate of nearly 20%.[12] Elevated PSA levels have been reported in patients with benign prostatic hyperplasia, prostatitis, and following prostate massage.[9] Furthermore, 5-alpha reductase inhibitors have been associated with an approximately 50% reduction in PSA, which may interfere with accurate screening.[9]

Risks associated with screening may also result from complications of a prostate biopsy, which include hematospermia and infection.[9]

Overdiagnosis is a significant concern because subsequent localized treatments may result in long-term erectile dysfunction, urinary incontinence, and bowel symptoms.[7]

Diagnosis and staging

Cancer screening programs are particularly important for early detection in conditions that are not generally associated with symptoms. Many patients with prostate cancer are asymptomatic for years while living with the disease. However, patients who develop large localized or regional tumors may present with changes in urination, hematuria, or hematospermia.

Symptoms are variable in patients with metastatic disease and depend on the site of metastases but may include pain, numbness, and fatigue.

Table 1. Select screening guidelines for prostate cancer

Guideline	Population	Screening recommendation	Screening test, interval, and referral for biopsy
U.S. Preventive Services Task Force	Men 55–69 years	The decision to screen should be individualized. Men should have an opportunity to discuss potential benefits and harms with their health care provider.	• PSA test without digital rectal exam • Periodic screening • No defined PSA threshold for biopsy referral
	Men ≥70 years or any age with a life expectancy of <10–15 years	Guideline recommends against PSA-based screening.	N/A
American Cancer Society	Men ≥40 years who have more than one first-degree relative (father or brother) with prostate cancer diagnosed before the age of 65 years	Men should have the opportunity to make an informed decision with their health care provider after receiving information about the potential benefits, harms, and uncertainties.	• PSA test with or without digital rectal exam • If PSA <2.5 ng/mL, screening intervals can be extended to every 2 years • If PSA ≥2.5 ng/mL, screening should be conducted yearly but consider risk factors • If PSA ≥4 ng/mL, patients should receive a referral and select patients should undergo a biopsy
	Men ≥45 years who are African American and/or have one first-degree relative (father or brother) with prostate cancer diagnosed before the age of 65 years		
	Men 50–69 years who are at average risk		
	Men ≥70 years or any age with a life expectancy of <10 years	Guideline recommends against PSA-based screening.	N/A
American Urological Association	Men 55–69 years	Men should participate in shared decision-making with their health care provider and proceed based on their values and preferences.	• PSA test; no digital rectal exam for primary screening • 2-year screening interval may be preferred over annual screening • Patient factors should be considered for biopsy rather than an absolute PSA threshold
	Men ≥70 years or any age with a life expectancy of <10–15 years	Guideline does not recommend routine PSA-based screening	N/A

Abbreviation used: PSA, prostate-specific antigen.
Sources: Adapted from References 7–9.

A further assessment should be completed when there is a suspicion of prostate cancer or in symptomatic patients. Such a workup includes a repeat PSA, digital rectal exam (DRE), and evaluation for benign disease.

Further evaluation may include a multiparametric MRI. When the suspicion for clinically significant prostate cancer is high, a transrectal ultrasound-guided biopsy should be completed (Figure 1).[10]

The most common cancer histology found in the prostate biopsy specimen is adenocarcinoma, which develops from the gland cells that secrete prostate fluid. A biopsy will also reveal the Gleason pattern, which plays a key role in staging and prognosis.

The Gleason system defines five histological growth patterns, which range from Gleason 1 (well-differentiated) to Gleason 5 (which is the least differentiated). The Gleason score is the sum of the two most common patterns (e.g., a primary pattern of 4 plus a secondary pattern of 3 would result in a Gleason score of 4 + 3 = 7).

In 2014, the International Society of Urological Pathology endorsed a Gleason Grade Group classification system which separates tumors into five categories based on Gleason scores (Table 2).[13]

In addition to the Gleason Grade Group, other factors in the American Joint Committee on Cancer (AJCC) prognostic group classification include PSA and Tumor, Node, Metastases staging.[14] However, unlike guidelines for many solid tumors that have incorporated AJCC staging recommendations, AJCC staging has not been widely adopted in national guidelines for prostate cancer.

Risk stratification tools have been developed by multiple organizations, but it remains unclear which model more accurately predicts prostate cancer death. The NCCN risk stratification model is commonly used in clinical practice to guide additional evaluations and therapies for localized prostate cancer (Table 3).[15]

Prevention strategies

Multiple chemoprevention strategies have been explored for prostate cancer.

The 5-alpha reductase inhibitors finasteride and dutasteride have been studied in two large, randomized trials.[16,17] The Prostate Cancer Prevention Trial (PCPT) enrolled 18,882 men ages ≥55 years with a PSA of ≤3.0 ng/mL.[16] Patients were randomized to receive finasteride 5 mg or placebo daily for 7 years.[16] Prostate cancer was detected in 18.4% of men randomized to finasteride versus 24.4% in the placebo group. However, the study also reported an increased risk of high-grade prostate cancer associated with the finasteride group (37.0% vs. 22.2% with a Gleason score of 7–10).[16] Sexual adverse effects were more common in the finasteride group.

The second study, known as the REDUCE trial, evaluated the impact of dutasteride on the incidence of prostate cancer.[17] In the study, a total of 6,729 men ages 50 to 75 years were randomized to dutasteride 0.5 mg or placebo daily for 4 years.[17] Prostate cancer was detected in 19.9% of men receiving dutasteride compared to 25.1% of those who received the placebo.[17] Similar to the PCPT, an increased incidence of high-grade prostate cancer was reported in the dutasteride arm during years 3 and 4 of treatment (12/2447 vs. 1/2343, with a Gleason score of 8–10).

Notably, no survival benefit was shown in either the PCPT or REDUCE trials. In a joint guideline from the American Society of Clinical Oncology and the American Urological Association, the expert panel recommends that asymptomatic men with a PSA ≤3 ng/mL who are regularly screened or anticipate screening may benefit from a discussion on the risks and benefits of 5-alpha reductase inhibitors to allow for informed decision-making.[18]

The Selenium and Vitamin E Prevention Trial (SELECT) was another large, randomized, placebo-controlled study that evaluated 35,533 men ages

Figure 1. Transrectal biopsy

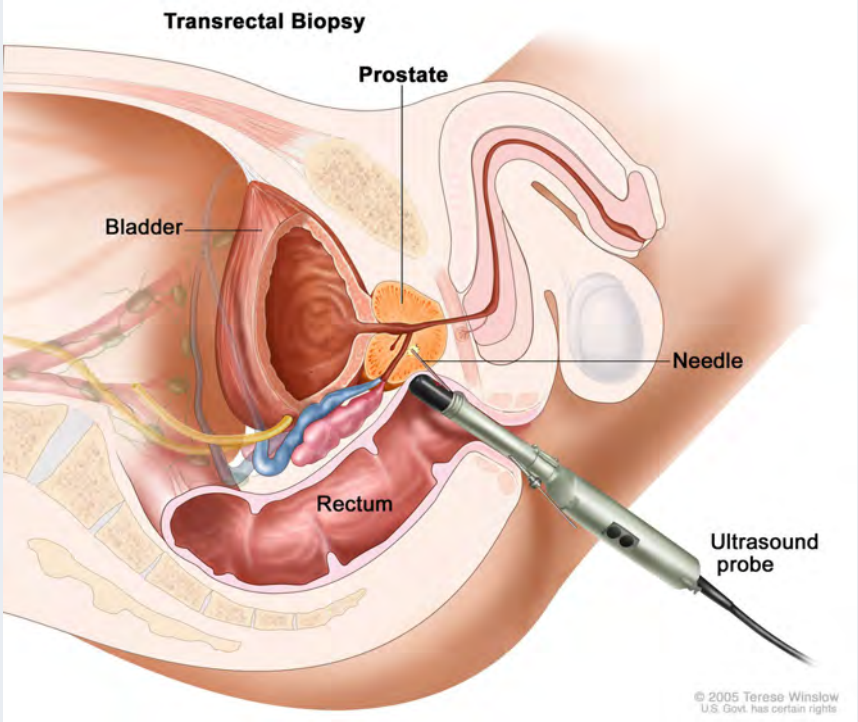

Table 2. Grade groups based on Gleason score and Gleason pattern

Grade group	Gleason score	Gleason pattern
1	≤6	3+3 (or less)
2	7	3+4
3	7	4+3
4	8	4+4, 3+5, 5+3
5	9 or 10	4+5, 5+4, 5+5

Source: Adapted from Reference 13.

Table 3. Risk stratification and clinical/pathologic considerations

Risk group		Considerations
Very low		■ Staging (e.g., cT1c) ■ Grade group ■ PSA ■ PSA density (PSA ÷ prostate volume) ■ % biospy cores positive
Low		
Intermediate	Favorable intermediate	
	Unfavorable intermediate	
High		
Very high		

Source: Adapted from Reference 15.

Table 4. Common pharmacologic treatments for prostate cancer

Drug class	Medication	Treatment settings[a]	Select notable toxicities	Additional considerations
Androgen deprivation therapy				
LHRH agonists	Leuprolide Gosereli	• Localized or regional disease • mCSPC • nmCRPC • mCRPC	• Hot flashes • Loss of libido • Erectile dysfunction • Shrinkage of the penis and testicles • Loss of muscle mass and strength • Fatigue • Anemia • Gynecomastia • Hair thinning • Osteoporosis • Altered mood • Obesity • Lipid abnormalities • Greater risk of diabetes • Greater risk for CVD • Injection site reactions (all products except relugolix)	• Available as long-acting injectable formulations • Testosterone flare/surge possible
LHRH antagonist	Degarelix	• Localized or regional disease • mCSPC • nmCRPC • mCRPC		• Available as a monthly injectable formulation
	Relugolix			• The only oral ADT option • Potential drug–drug interactions • Minimal data for concurrent use with other prostate cancer therapies
Antiandrogens				
First-generation antiandrogens	Bicalutamide Flutamide Nilutamide	• Localized or regional disease • Metastatic disease (select circumstances)	• Gynecomastia • Hepatotoxicity • Cardiac events • Visual changes (nilutamide)	• Oral • Bicalutamide primarily used in clinical practice
Second-generation antiandrogens	Apalutamide	• mCSPC • nmCRPC	• Dermatologic toxicity • Falls and fractures • Seizures • Thyroid dysfunction • Cardiac events	• Oral • Significant drug–drug interactions
	Darolutamide	• mCSPC • nmCRPC	• Seizures • Cardiac events	• Oral • Significant drug–drug interactions
	Enzalutamide	• mCSPC • nmCRPC • mCRPC	• Hot flashes • Falls and fractures • Seizures • PRES • Cardiac events	• Oral • Significant drug–drug interactions
CYP17 inhibitor	Abiraterone	• Very high risk or regional disease (select patients) • Pelvic recurrence after RP • mCSPC • mCRPC	• Adrenocortical insufficency • Mineralocorticoid excess • Hepatotoxicity	• Given orally in combination with steroids • Significant drug–drug interactions • Multiple formulations

≥55 years (Black men aged ≥50 years) with a PSA ≤4 ng/mL.[19] In the study, men were randomly assigned to one of four treatment groups: selenium 200 µg/day plus vitamin E placebo, vitamin E 400 IU/day plus selenium placebo, selenium 200 µg/day plus vitamin E 400 IU/day, or selenium placebo plus vitamin E placebo.[19] In the double placebo group, 529 men developed prostate cancer compared to 620 men in the vitamin E group (hazard ratio [HR] 1.17; 99% CI, 1.004–1.36, P = 0.008), 575 men in the selenium group (HR 1.09; 99% CI, 0.93–1.27, P = 0.18), and 555 in the selenium plus vitamin E group (HR 1.05; 99% CI, 0.89–1.22, P = 0.46).[19] The authors concluded that in healthy men, dietary supplementation with vitamin E significantly increased the risk of prostate cancer.[19]

Treatment considerations

The choice of treatment for patients with non–high-grade localized adenocarcinoma of the prostate is based on a shared decision-making approach which incorporates education on the potential treatment advantages and disadvantages, in addition to patient specific factors and preferences.

Possible treatment options should be appropriate based on risk stratification and anticipated patient survival. Considerations include external beam radiation therapy, radical prostatectomy, active surveillance, and observation. Radiation therapy and a radical prostatectomy are often associated

Table 4. Common pharmacologic treatments for prostate cancer

Drug class	Medication	Treatment settings[a]	Select notable toxicities	Additional considerations
Cytotoxic chemotherapy				
Antimicrotubule agents (taxanes)	Docetaxel	• mCSPC • mCRPC	• Myelosuppression • Peripheral neuropathy • Infusion-related reactions • Fluid retention (docetaxel)	• Given I.V. in combination with prednisone
	Cabazitaxel	• mCRPC		
Anthracenedione	Mitoxantrone	• mCRPC for palliation only	• Myelosuppression • Cardiotoxitiy • Blue-green coloration	• No overall survival benefit but improved quality of life • Given I.V. in combination with steroids
Radiopharmaceuticals				
Radium Ra 223 dichloride		• mCRPC with symptomatic bone metastases and no known visceral disease	• Myelosuppression	• I.V. • Precautions for radiopharmaceuticals
Lutetium Lu 177 vipivotide tetraxetan		• PSMA-positive mCRPC	• Myelosuppression • Renal toxicity • Xerostomia	
Targeted therapies				
PARP inhibitors	Olaparib	• mCRPC HRRm	• Secondary malignancy • Thromboembolic events • Nausea/vomiting • Myelosuppression	• Oral • Reversible increase in SCr thought to be related to an inhibition of renal transporters
	Rucaparib	• mCRPC, BRCA mutation	• Secondary malignancy • Nausea/vomiting • Myelosuppression	
Immunotherapies				
Autologous cellular immunotherapy	Sipuleucel-T	• mCRPC, asymptomatic or minimally symptomatic	• Infusion-related reactions • Chills, pyrexia, headache	• I.V., autologous use only
Immune checkpoint inhibitor	Pembrolizumab	• mCRPC, MSI-H, dMMR, or TMB ≥10 mut/Mb	• Immune-related adverse events	• I.V.

[a] Includes both FDA-approved indications and nonlabeled uses supported in national guidelines

Abbreviations used: ADT, androgen deprivation therapy; CVD, cardiovascular disease; dMMR, mismatch repair deficient; HRRm, homologous recombination repair gene-mutated; I.V., intravenous; LHRH, luteinizing hormone releasing hormone; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; MSI-H, microsatellite instability-high; nmCRPC, nonmetastatic castration-resistant prostate cancer; PRES, posterior reversible encephalopathy syndrome; RP, radical prostatectomy; TMB, tumor mutational burden.

Sources: Adapted from FDA-approved product labeling and Reference 15.

with detrimental urologic effects and sexual dysfunction.

Active surveillance

The goal of active surveillance is to avoid or delay unnecessary treatments and their associated toxicities in patients with indolent prostate cancer. Those eligible for active surveillance programs may safely avoid treatment for at least 10 years.[20]

Quality of life can be maintained during this time. Although some patients will undergo treatment by 10 years, the impact on cure rate is likely not affected and the risk of metastasis is minimal.[15]

At minimum, principles of an active surveillance program include[15]

- PSA check: no more frequent than every 6 months (unless clinically indicated)
- DRE check: no more frequent than every 12 months (unless clinically indicated)
- Prostate biopsy: no more frequent than every 12 months (unless clinically indicated)

Patients who have a life expectancy of <10 years should transition to observation.[15] Patients opting for observation should undergo monitoring with a history and physical no more than every 12 months until symptoms develop. Biopsies are generally not considered part of observation programs. Observation provides the same advantages as active surveillance but with the added benefit of evading unnecessary confirmatory testing.

Pharmacologic treatment options

Over the past decade, the prostate cancer treatment landscape has continued to evolve and now includes a multitude of pharmacologic options (Table 4).

ADT

Androgen deprivation therapy (ADT) remains the treatment backbone of prostate cancer and is used in both the localized and metastatic settings.

The most commonly used agents in clinical practice are the luteinizing hormone-releasing hormone (LHRH) agonists. These agents produce an initial increase in luteinizing hormone and follicle stimulating hormone and an initial rise in testosterone. However, as the result of a negative feedback loop, continuous administration of the agonist will ultimately result in a reduction of testosterone to below castrate levels (<50 ng/dL).

Conversely, LHRH antagonists block the pathway, thus causing an immediate reduction in testosterone without the flare or surge reported with LHRH agonists. Although the clinical significance has been debated, the flare phenomenon may result in a temporary worsening of urinary symptoms, worsening pain in patients with bone metastases, and risk of a cord impingement in patients with spinal metastases. Concurrent use of bicalutamide at the start of the LHRH agonist may negate these concerns.

For many patients, long-term testosterone suppression has a significant impact on quality of life. Notable adverse effects associated with testosterone suppression include the following:[15]

- Hot flashes
- Erectile dysfunction
- Loss of muscle mass and strength
- Anemia
- Hair thinning
- Altered mood
- Lipid abnormalities
- Greater risk for cardiovascular disease
- Shrinkage of the penis and testicles
- Fatigue
- Gynecomastia
- Osteoporosis
- Obesity
- Greater risk for diabetes

Antiandrogens

First-generation antiandrogens (i.e., bicalutamide, nilutamide, and flutamide) work by binding and inhibiting the androgen receptor. Although these agents are significantly less expensive compared to later generation products, disadvantages related to their mechanism have limited use in clinical practice. For example, partial androgen agonism has been associated with resistance.[21]

Second-generation antiandrogens (i.e., enzalutamide, darolutamide, apalutamide) block the androgen receptor and inhibit translocation to the nucleus but do not have agonistic properties.

Another antiandrogen, abiraterone, inhibits CYP17 which is an enzyme involved with androgen biosynthesis. Blocking the CYP17 pathway inhibits the formation of testosterone precursors. Notably, inhibiting CYP17 also suppresses cortisol production overall and a rise in cortisol precursors with mineralocorticoid activity results. Therefore, prednisone must be given concurrently with abiraterone to serve as a glucocorticoid replacement and to reduce adverse effects associated with mineralocorticoid excess.

Abiraterone and the second-generation antiandrogens are often referred to as novel hormonal therapies.

Cytotoxic chemotherapy

Cytotoxic chemotherapy continues to have a role in the treatment of metastatic prostate cancer.

The taxane derivatives docetaxel and cabazitaxel have the most utility in treating prostate cancer and function as antimicrotubule agents. Although both have the same mechanism of action, cabazitaxel has been shown to overcome docetaxel resistance through its poor affinity for P-glycoprotein (P-gp).[22]

P-gp is a drug efflux transporter that is expressed on some cancer cells. Tumors expressing P-gp will generally develop resistance to drugs with high P-gp affinity such as docetaxel.

Notable toxicities with docetaxel and cabazitaxel include myelosuppression, neuropathy, and infusion-related reactions.

Radiopharmaceuticals

Two radiopharmaceuticals are FDA-approved for the treatment of patients with metastatic prostate cancer. While these agents provide an innovative mechanism for DNA damage and cell death, adverse effects can be significant.

Radium Ra 223 dichloride is an alpha particle–emitting isotope which targets bone metastases by mimicking calcium to form bone complexes. Based on its mechanism, it is only approved for patients with castration-resistant prostate cancer (CRPC) with symptomatic bone metastases and no known visceral disease. Myelosuppression is a common toxicity associated with radium Ra 223 dichloride.

Lutetium Lu 177 vipivotide tetraxetan (also called ^{177}Lu-PSMA-617) is a radioligand that binds to prostate-specific membrane antigen (PSMA), which is highly expressed on prostate cancer

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

cells. After binding, beta-minus emission releases radiation to the cancer cells.

FDA has approved lutetium Lu 177 vipivotide tetraxetan for PSMA-positive metastatic CRPC (mCRPC). PSMA-positive mCRPC is defined as having at least one tumor lesion on positron emission tomography using gallium Ga 68 gozetotide. Toxicities include myelosuppression and renal impairment. Notably, salivary glands have shown a high PSMA-ligand uptake, and subsequent radiation-mediated toxicity to the glands is a concern.[23] Xerostomia has been reported in up to 39% of patients.

In addition to medication-specific considerations, special precautions must be applied to all radiopharmaceuticals to minimize unintended exposure.

Targeted therapies

FDA has approved two poly (ADP-ribose) polymerase (PARP) inhibitors for the treatment of select men with metastatic prostate cancer.

PARP enzymes play a key role in the repair of DNA damage. Specifically, PARP binds to single-strand DNA breaks and recruits other enzymes to repair the DNA damage. However, if a single strand is not repaired by PARP during replication, a double-strand break may result. A normal cell could then repair the double-strand DNA break through homologous recombination mechanisms, ultimately resulting in cell survival. Since *BRCA1* and *BRCA2* genes encode key components of the homologous recombination repair pathways, BRCA mutations inherently result in deficiencies in DNA repair. This vulnerability forms the basis for the concept of synthetic lethality.

The use of PARP inhibitors for select patients with prostate cancer is well-established, but applicability for their widespread use in this population has yet to be determined. Olaparib is approved for the treatment of homologous recombination repair gene–mutated mCRPC following progression on a novel hormonal agent, while rucaparib is approved in patients with *BRCA*-mutated mCRPC following treatment with an antiandrogen and a taxane.

Adverse effects associated with PARP inhibitors include nausea/vomiting, myelosuppression, and secondary malignancies.

Immunotherapies

Despite the drastic survival benefits of immunotherapies in multiple solid tumors, positive outcomes in prostate cancer have been limited.

Sipuleucel-T, an autologous cellular therapy, was one of the first available immunotherapies, but its approval did not come without controversary.[24] The debate stemmed from subpar trial design and failure to meet statistical significance for the primary endpoint. Nevertheless, sipuleucel-T is an available option in the treatment arsenal for patients with mCRPC who are asymptomatic or minimally symptomatic.

Sipuleucel-T is generally well tolerated but infusion-related reactions and flu-like symptoms are common.

Pembrolizumab is an immune checkpoint inhibitor that works by binding the programmed death–1 receptor and blocking ligand interaction. As a result, immune downregulation is reversed, allowing for an antitumor immune response. Pembrolizumab holds a tissue/site agnostic approval as subsequent therapy for microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) solid tumors.

A subsequent FDA approval expanded pembrolizumab's use to patients with tumor mutation burden-high (TMB-H) solid tumors. Tumors with these characteristics have been shown to be more responsive to immune checkpoint inhibitors. Significant improvements in overall survival and durable benefits have been demonstrated. The NCCN guidelines suggest pembrolizumab as a treatment option for patients with MSI-H, dMMR, or TMB-H mCRPC following prior docetaxel and novel hormonal therapy.[15]

Treatment guidelines and select landmark trials

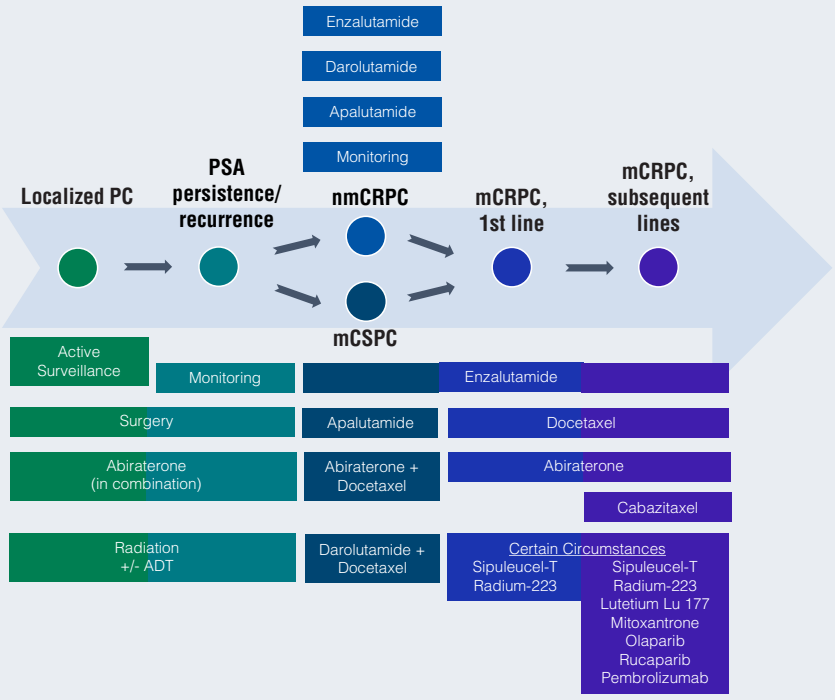
Recent national guidelines have emphasized risk stratification in an effort to avoid overtreatment of indolent disease while appropriately treating those at risk of disease progression.

Pharmacologic treatments have trended earlier in the disease course, and new combination regimens have emerged. Figure 2 reviews treatment options across the prostate cancer continuum. Select landmark trials that have most recently impacted national guidelines are summarized below.

Localized prostate cancer

Abiraterone was originally approved in 2011 for the treatment of patients with mCRPC. Investigators on the STAMPEDE platform protocol recently published a meta-analysis of two randomized, Phase 3 trials evaluating abiraterone with or without enzalut-

Figure 2. Treatment options across the prostate cancer continuum



amide in high-risk nonmetastatic prostate cancer, which was defined as either node positive or as node negative with at least two high-risk features.[25] Local radiotherapy was required for node negative and encouraged for node positive disease.

Patients in one trial were randomized to the control arm (ADT alone) or the abiraterone arm (ADT plus abiraterone 1,000 mg orally daily plus prednisolone 5 mg orally daily).[25] In the second trial, the experimental arm added enzalutamide (160 mg orally daily) to the regimen.[25] The primary endpoint was metastasis-free survival.[25]

A total of 1,974 patients were randomized: 455 to the control group and 459 to combination therapy in the first trial, and 533 to the control group and 527 to combination therapy in the second trial.[25] Metastasis-free survival was significantly longer in the combination therapy groups compared to the control group ($P < 0.0001$) and the 6-year metastasis-free survival rate was 82% in the combination group versus 69% in the control group.[25] Overall survival (OS) was also statistically improved with the combination group ($P < 0.001$).[25] However, there was no statistical differences in metastasis-free survival with the addition of enzalutamide ($P = 0.90$).[25]

As a result of these data from the STAMPEDE trial, the NCCN guidelines have been updated to incorporate abiraterone as an option for select patients with very high-risk or regional disease.[15]

mCSPC

The ARASENS trial evaluated the use of darolutamide or placebo plus both ADT and docetaxel in patients with metastatic castration-sensitive prostate cancer (mCSPC).[26] The international, double-blind, Phase 3 trial included 1,306 patients who were randomized 1:1 to receive darolutamide (600 mg orally twice daily) or a matching placebo in addition to the standard of care (ADT plus docetaxel). The primary endpoint was OS. At a median follow-up of over 40 months, the OS was significantly improved in the darolutamide arm compared to the placebo arm ($P < 0.001$).[26]

Benefits of darolutamide were consistent with respect to secondary endpoints and for prespecified subgroups.[26] No new safety signals were reported with the combination.[26]

The PEACE-1 trial evaluated the safety and efficacy of abiraterone plus prednisone with or without radiotherapy in addition to standard of care (ADT alone or with docetaxel) in patients with de novo mCSPC.[27] Patients were randomized 1:1:1:1 to one of the following groups: standard of care; standard of care plus radiotherapy; standard of care plus abiraterone plus prednisone; or standard of care plus radiotherapy plus abiraterone.[27] The open-label trial enrolled 1,173 patients and the co-primary endpoints were radiographic progression-free survival (PFS) and OS. In the overall population, patients receiving abiraterone had an improvement in radiograph PFS ($P < 0.0001$) and OS ($P = 0.030$). A higher number of adverse events were reported in patients receiving abiraterone compared to those who did not (63% vs. 52%, respectively).

Based on the results of the ARASENS and PEACE-1 trials, the NCCN guidelines now include ADT plus docetaxel and either darolutamide or abiraterone as options for patients with mCSPC.

mCRPC

In March 2022, FDA approved lutetium Lu 177 vipivotide tetraxetan for the treatment of PSMA-positive mCRPC following an antiandrogen and taxane-based chemotherapy.

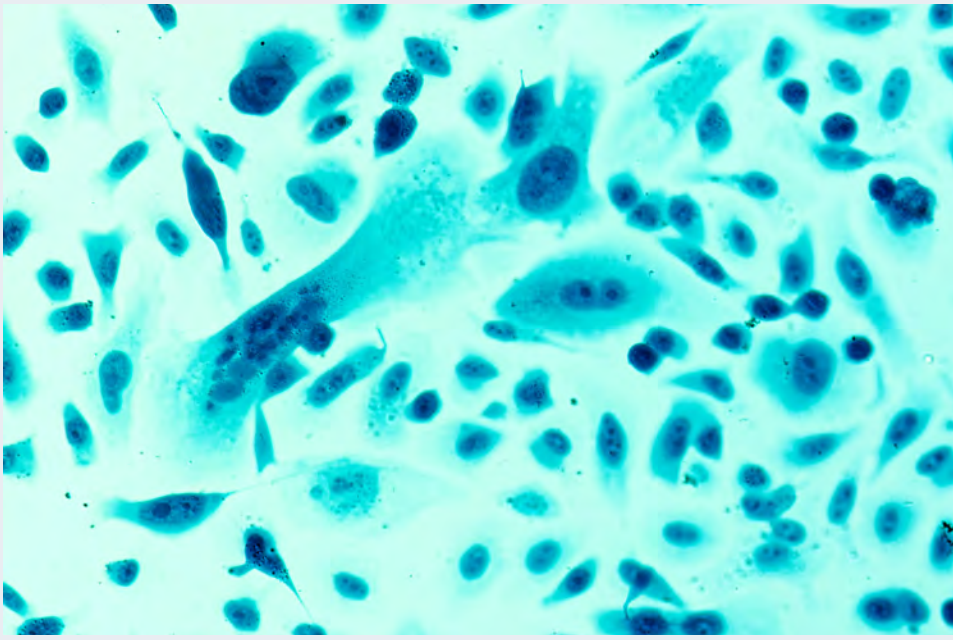
The approval was based on the results from the VISION trial, an open-label, Phase 3 study. A total of 831 patients with PSMA-positive mCRPC were randomized 2:1 to receive lutetium Lu 177 vipivotide tetraxetan (7.4 GBq every 6 weeks for four to six infusions) plus standard of care or standard of care alone. The primary endpoints were imaging-based PFS and OS. Compared to standard of care, lutetium Lu 177 vipivotide tetraxetan significantly prolonged PFS (median 8.7 vs. 3.7 months) and OS (median 15.3 vs. 11.3 months).

As a result of the VISION trial, lutetium Lu 177 vipivotide tetraxetan was incorporated into NCCN guidelines as an option for patients with mCRPC

following prior docetaxel and prior novel hormonal therapy.[15]

Conclusion

Given the often indolent nature of prostate cancer combined with the challenging adverse effects of treatment, health care professionals must prioritize shared decision-making. Treatment decisions should be guided by a thorough understanding of benefits and risks for a particular patient. Patients considering PSA-based screening and patients diagnosed with prostate cancer may need assistance in navigating the complex options. Fortunately, pharmacists have the knowledge and expertise to participate in shared decision-making and can help guide patients through the challenging journey ahead. ■



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Postassessment questions

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 reinforce the learning opportunity. There is only one correct answer to each question.

1. According to the American Cancer Society, a male with a life expectancy of 30 years who has two first-degree relatives who were diagnosed with prostate cancer at a young age should have the opportunity to make an informed prostate cancer screening decision with their health care provider starting at what age?

a. ≥40 years
b. ≥45 years
c. 50–69 years
d. ≥70 years

2. A patient inquires about the potential benefits of selenium and vitamin E for the prevention of prostate cancer. Which of the following most accurately summaries the results of the SELECT trial?

a. More men developed prostate cancer in the placebo arm compared to the selenium arm.
b. Compared to placebo, selenium plus vitamin E significantly reduced the risk of prostate cancer.
c. Compared to placebo, vitamin E significantly increased the risk of prostate cancer.
d. There was no difference in the risk of prostate cancer between all four treatment arms.

3. Xerostomia is a significant adverse effect commonly reported with which prostate cancer therapy?

a. Radium Ra 223 dichloride
b. Lutetium Lu 177 vipivotide tetraxetan
c. Docetaxel
d. Olaparib

4. According to the NCCN guidelines, which novel hormonal therapy may be given as part of a combination regimen for select patients with localized prostate cancer?

a. Abiraterone
b. Enzalutamide
c. Darolutamide
d. Apalutamide

5. Based on the goals of active surveillance, which of the following parameters would be most appropriate to include in an active surveillance program?

a. PSA check monthly, DRE monthly, prostate biopsy monthly
b. PSA check every 3 months, DRE every 6 months, prostate biopsy every 6 months
c. PSA check every 6 months, DRE every 6 months, prostate biopsy every 6 months
d. PSA check every 6 months, DRE every 12 months, prostate biopsy every 12 months

6. Steroids must be given concurrently with which prostate cancer therapy to provide a glucocorticoid replacement and to reduce the adverse effects associated with mineralocorticoid excess?

a. Docetaxel
b. Abiraterone
c. Sipuleucel-T
d. Bicalutamide

7. Based on the results of the ARASENS study, which combination regimen is now included as an option in the NCCN Guidelines for the treatment of mCSPC?

a. ADT plus docetaxel and abiraterone
b. ADT plus abiraterone and enzalutamide
c. ADT plus docetaxel and darolutamide
d. ADT plus cabazitaxel and apalutamide

8. Testosterone suppression resulting from ADT is commonly associated with which of the following adverse effects?

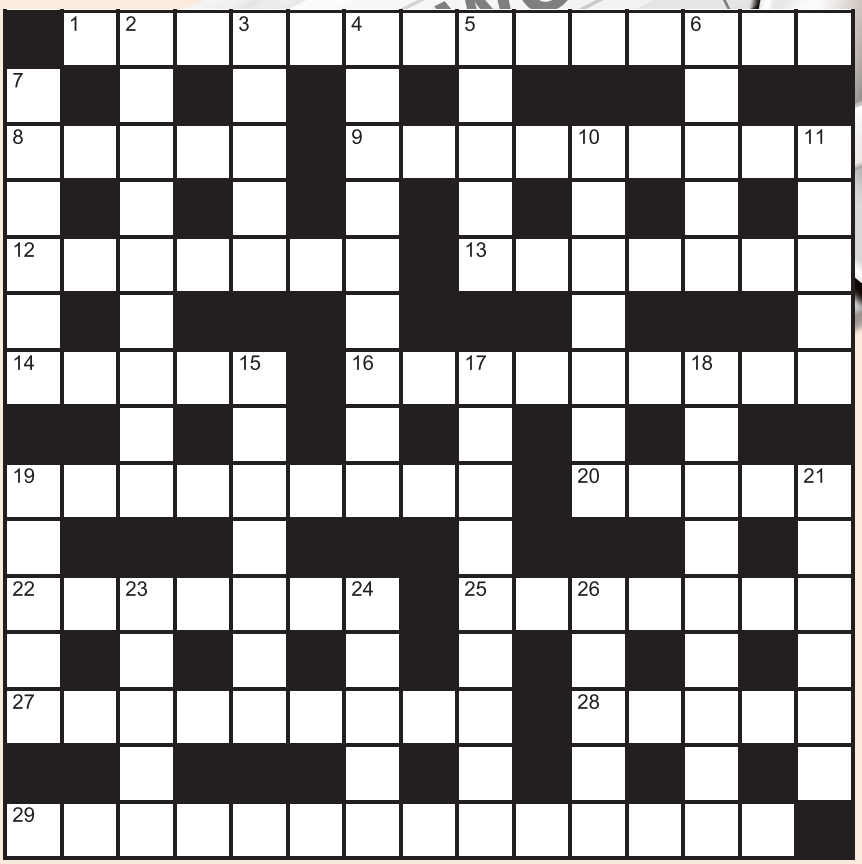
a. Hot flashes
b. Weight loss
c. Increased muscle mass
d. Improvement in bone mineral density

9. A 42-year-old African American male inquires about his risk for prostate cancer. Which of the following is true regarding prostate cancer risk factors?

a. A younger age is associated with a higher risk of prostate cancer.
b. A family history of prostate cancer is unlikely to increase risk.
c. Germline mutations have not been associated with prostate cancer risk.
d. Non-Hispanic Black men are more likely than non-Hispanic white men to develop prostate cancer.

10. A patient is requesting more information regarding the pros and cons of taking finasteride for the prevention of prostate cancer. Which of the following most accurately summaries the results of the PCPT trial?

a. Prostate cancer was detected in more men randomized to finasteride compared to placebo, but the risk of high-grade prostate cancer was reduced.
b. Prostate cancer was detected in fewer men randomized to finasteride compared to placebo, but the risk of high-grade prostate cancer was increased.
c. Prostate cancer was detected in more men randomized to finasteride compared to placebo, and the risk of high-grade prostate cancer was increased.
d. Prostate cancer was detected in fewer men randomized to finasteride compared to placebo, and the risk of high-grade prostate cancer was reduced.



Across

1 False or misleading data or advice
8 Critical
9 Pharmacists must be good _____ to notice patient symptoms
12 Arteries that carry blood to the brain
13 Alpine vocalist
14 Prefix meaning below, often used with red
16 Incongruous
19 Fetal cell
20 Nikola who was a rival of Thomas Edison
22 Driving force
25 Bank book entry
27 Sudden increase in occurrences of diseases
28 Hideouts
29 Anorexia or bulimia, for example

Down

2 Pharmacists are compounding this NSAID for pediatric patients
3 Unreactive
4 Patients trying to lose weight are often advised to keep this
5 Hazardous
6 Perfect, flawless
7 Chinese discipline of meditative movements
10 This kind of energy causes sunburn
11 Often require bandages
15 A techie is almost always an early _____
17 The number of these caused by opioids continues to increase
18 The "O" in OCD
19 Kind of acid that make up proteins
21 Neurodevelopmental disorder with a spectrum
23 Small, in legal cases
24 Burn caused by steam
26 _____ opposite

Solution is available online at pharmacytoday.org.