Pharmacy Today
An official publication of the **American Pharmacists Association**
MAY 2024

# PSYCHEDELICS AND ALTERNATIVES TO TREAT PSYCHIATRIC CONDITIONS

**PEDIATRICS**
**The importance of weight-based dosing**

**CONTROLLED SUBSTANCES**
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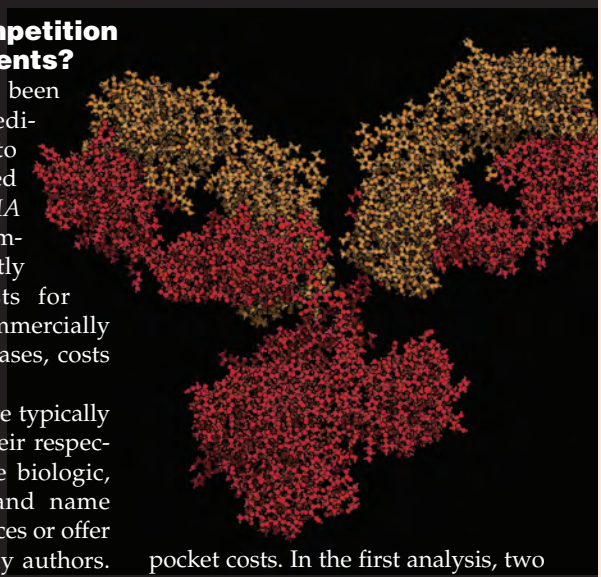
CONTINUING PHARMACY EDUCATION
**CPE**
A patient's journey with migraine

APhA

# BulletinToday

## Does biosimilar competition lower costs for patients?



Biosimilars have typically been viewed as cost-saving medications, but according to results of a study published on March 29, 2024, in *JAMA Health Forum*, biosimilar competition did not consistently lower out-of-pocket costs for outpatients who were commercially insured. In fact, in some cases, costs even increased.

"Prices for biosimilars are typically 15% to 35% lower than their respective brand-name reference biologic, and can prompt the brand name manufacturers to lower prices or offer discounts," noted the study authors. What they wanted to find out was whether biosimilar competition lowers costs for patients.

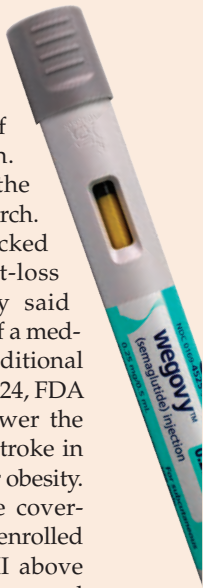
The researchers conducted a cohort study using a national commercial claims database and identified the out-of-pocket costs for those who were commercially insured across 7 physician-administered biologics with a biosimilar available in the United States from January 2009 through March 2022. The biologics included filgrastim, infliximab, pegfilgrastim, epoetin alfa, bevacizumab, rituximab, and trastuzumab. The primary outcome included out-of-pocket costs for the patient, such as deductible, copayment, and coinsurance.

Researchers performed two analyses to measure the association between biosimilar competition and out-of-pocket costs. In the first analysis, two biologics, rituximab and trastuzumab, were the only ones that showed significantly lower mean nonzero annual out-of-pocket spending after 2 years of biosimilar competition. The other drugs were either higher in cost or did not yield significant changes. In the second analysis, researchers found that 28% of the reference biologic claims and 17% of biosimilars had nonzero out-of-pocket costs, but after adjustment, biosimilars were more likely to have nonzero out-of-pocket claims compared to the reference product.

An important takeaway for policymakers, said the study authors, is to advocate for more targeted policy interventions that make biologics and biosimilars affordable and accessible to patients who need them. ■

## Some Medicare health plans to start paying for weight-loss drugs

CVS Health, Kaiser Permanente, and Elevance Health will be the first major insurers in the country to cover the GLP-1 receptor agonist semaglutide (Wegovy—Novo Nordisk) for a segment of the Medicare population. The announcement by the companies came in late March.




Medicare has been blocked from paying for weight-loss drugs, but CMS recently said exceptions might be made if a medication is approved for additional indications. On March 8, 2024, FDA cleared semaglutide to lower the risk of heart disease and stroke in patients with overweight or obesity.

To qualify for Medicare coverage, beneficiaries must be enrolled in Part D and have a BMI above a set threshold plus documented heart disease. Elevance Health said they will pay for the GLP-1 receptor agonist for patients in the commercial insurance space who match this profile.

Expanded coverage will come as a relief to many patients who often pay upwards of $1,000 out of pocket for semaglutide. However billions of dollars spent on semaglutide could be racked up even as health plans struggle to keep costs in check. ■

## Hormonal contraception will be available without a prescription in New York pharmacies

The New York State Department of Health issued an order in late March to formally implement a new law establishing access to hormonal contraception from pharmacists without a physician's order.

Both residents of New York and nonresidents can receive a 1-year supply of oral contraception, vaginal rings, or patches from participating pharmacies, which will provide consultation and counseling services.

State officials estimate that 85% of pharmacies will take up the new authority, which seeks not only to eliminate barriers to access, but to protect reproductive rights in the post-Roe landscape. More than 20 states have restricted or completely outlawed abortions since the U.S. Supreme Court repealed the landmark ruling that empowered women with a constitutional right to terminate a pregnancy. At least two dozen other states have preceded New York in granting pharmacists some capacity to dispense contraception without a prescription. ■

## Study links heart failure risk to e-cigarette use

Data from an NIH-led study found that people who used e-cigarettes were 19% more likely to develop heart failure compared with people who never vaped.

Researchers used data from surveys and EHRs in the NIH-run All of Us study of 175,667 study participants. The average age of participants was 52 years, and over half were female.

In all, 3,242 participants developed heart failure within a median follow-up period of 45 months. The researchers accounted for demographic and socioeconomic factors, heart disease risk factors, and participants' past and present use of other substances.

The connection between e-cigarettes and heart failure was not affected by participants' age, sex, or smoking status, noted researchers.

"More and more studies are linking e-cigarettes to harmful effects and finding that it might not be as safe as previously thought," said Yakubu Bene-Alhasan, MD, the study's lead author in an American College of Cardiology (ACC) news release. "The difference we saw was substantial. It's worth considering the consequences to your health, especially with regard to heart health."

The findings were presented at the ACC's Annual Scientific Session on Sunday, April 7, 2024, in Atlanta, GA. ■

## Model sets out to tackle CVD disparities through pharmacy team partnerships

CDC, in partnership with APhA, has announced the teams that will be part of a project to advance health equity and prevent heart disease and stroke in the United States.

The Community of Practice Teams are part of the Advancing Health Equity and Pharmacy-Based Strategies, Pharmacists Patient Care Services and Support Services project. Through an application process, teams were selected from state and local health departments, state pharmacy associations, professional organizations, colleges of pharmacy, pharmacy practice settings, and community-based organizations.

Six teams in total have been selected to participate in the project based on their composition, qualifications, and commitment to CVD prevention. The teams have a goal to use pharmacy-based strategies to address racial and ethnic disparities in CVD risk factors, prevalence, and outcomes. ■

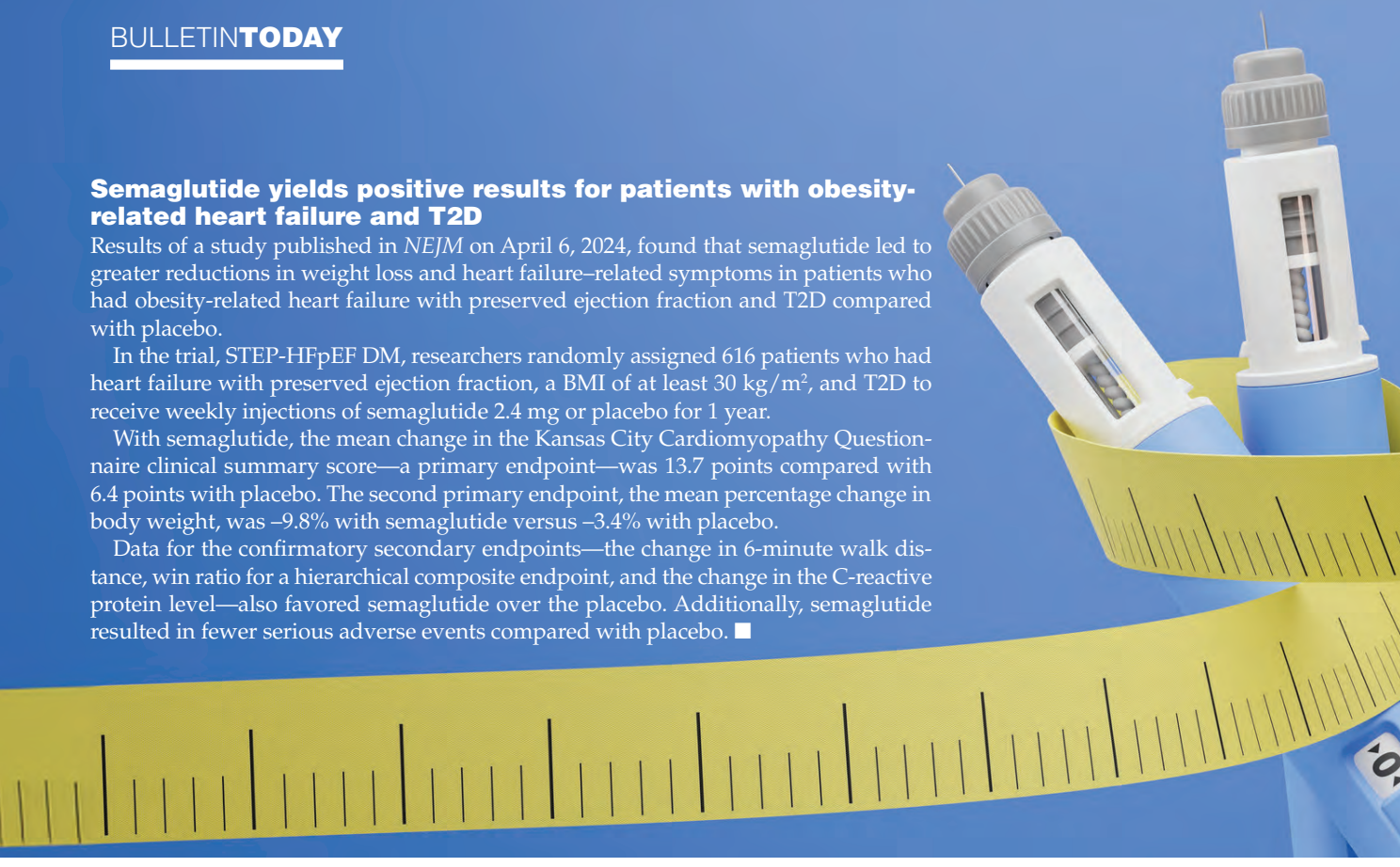
## Semaglutide yields positive results for patients with obesity-related heart failure and T2D

Results of a study published in *NEJM* on April 6, 2024, found that semaglutide led to greater reductions in weight loss and heart failure–related symptoms in patients who had obesity-related heart failure with preserved ejection fraction and T2D compared with placebo.

In the trial, STEP-HFpEF DM, researchers randomly assigned 616 patients who had heart failure with preserved ejection fraction, a BMI of at least 30 kg/m$^2$, and T2D to receive weekly injections of semaglutide 2.4 mg or placebo for 1 year.

With semaglutide, the mean change in the Kansas City Cardiomyopathy Questionnaire clinical summary score—a primary endpoint—was 13.7 points compared with 6.4 points with placebo. The second primary endpoint, the mean percentage change in body weight, was –9.8% with semaglutide versus –3.4% with placebo.

Data for the confirmatory secondary endpoints—the change in 6-minute walk distance, win ratio for a hierarchical composite endpoint, and the change in the C-reactive protein level—also favored semaglutide over the placebo. Additionally, semaglutide resulted in fewer serious adverse events compared with placebo. ■



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CPE



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## Take the Crossword Challenge

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*See solution at pharmacytoday.org*




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## Drugs & Diseases



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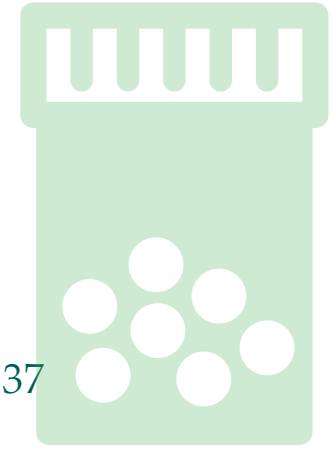
## Practice & Trends



## Health Systems





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# Mental health challenges: Are psychedelics the answer?

Psychedelics derived from plants, such as mescaline and psylocibin, have been used by indigenous peoples as part of religious rites for centuries, and more recently by patients seeking relief from PTSD and severe depression, despite their potentially harmful effects.

If approved by FDA this fall, Lykos Therapeutics' midomafetamine (MDMA) will become the first FDA-approved psychedelic therapy. Lykos Therapeutics is seeking authorization to treat PTSD in combination with psychotherapy…but keep an eye out for more psychedelic drug approvals for other indications on the horizon.

This month's *Pharmacy Today* cover story takes a deep dive into psychedelics. It is no longer a question of whether or not psychedelic medicines will join our treatment armamentarium, but rather when they will do so. Psylocibin, an agent naturally found in mushrooms, is undergoing clinical trials for treatment of severe depression and may be approved in the coming years. Ketamine, classified as a dissociative drug, is already being used as an adjuvant to psychotherapy.

These types of drugs have two primary effects: neuroplastic changes to repair or reset broken or disrupted neural networks and psychedelic effects. Researchers hope that these combined actions may ultimately achieve improved therapeutic outcomes with fewer adverse effects. Research is underway to tease out the optimal drug and/or combination of medications and psychotherapy to determine if the neuroplastic and psychedelic effects of these agents can and should be separated, and, if so, how best to do this.

In this issue of *Today*, you'll also learn more about using cranberry for UTIs, how Xolair (omalizumab—Genentech) works to address food allergies, and how gabapentin may worsen COPD symptoms. You'll also get the latest on preventing medication errors with reconstituted products and stay current with your CPE with this month's article on migraine.

While we wait for these emerging psychedelic medications to become more mainstream, pharmacists can prepare to answer patients' questions. Concerns may range from curiosity about others who have taken similar medications to a desire to learn about clinical trials or patient support organizations. Encourage patients to talk to you and their other health care providers before starting or stopping any new medication(s).

Have a great *Today*! ■

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***Pharmacy Today* editor in chief**

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PharmD, FAPhA, FNAP, FFIP
Executive vice president and CEO of APhA

# It's time to stop requiring certificate training in state regulations

My columns in *Pharmacy Today* and my CEO blogs all share one common thread: truth spoken honestly and sincerely, even if it isn't easy to write or easy to read. And I'm going to write today about something that I feel deep down needs to be said: pharmacists, be careful what you ask for from your state regulators and legislators.

I don't know who first coined the term, but there is without question a "law of unintended consequences," referring to the unexpected results of an action taken. Here's one prime example. Pharmacists in a state want the authority to prescribe HIV PrEP and PEP after conducting an HIV test and providing counseling on that test. In the process of negotiating with the legislature for this authority, the pharmacy association says "Look, we are so confident that our pharmacists will do a good job no matter what; however, we'll go ahead and put a provision in the law that requires pharmacists to complete a certificate program in order to provide the service." Also, nothing in the law that was passed addressed payment for the services of the pharmacist. The unintended consequences: pharmacists aren't interested in providing a service for which they can't get paid, and we've created an unnecessary hurdle to patient access to care by requiring pharmacists to jump through one more educational hoop.

My longtime friend and former APhA President Marialice Bennett, BSPharm, RPh, FAPhA, famously said "the profession of pharmacy is just one CE course away from being able to do anything!" She's right! What other health profession places condition-specific or situation-specific educational requirements on the health care professionals licensed in their state? Can't think of one? Neither can I!

We've done this to ourselves. And APhA and other national and state pharmacy associations are largely to blame for it.

Yes, I said it. We are to blame for it.

It was a good idea 30 years ago when immunizations became the first large-scale attempt at engaging pharmacists in nondispensing services in the community practice setting. At that time, you'd have been hard-pressed to find a pharmacist with any training in vaccines and immunization practice.

Unfortunately, by putting requirements that pharmacists need to complete certificate training in vaccines into state practice acts, we've set a precedent of expectation among lawmakers, physicians, and health systems that pharmacists need additional training anytime they plan to take on added responsibilities beyond our stereotypical dispensing activities.

If you don't believe this to be true, just look at the recent efforts to expand pharmacists' scope into point of care testing, HIV testing and prevention, primary care prescribing, etc. Several states have adopted laws adding more training requirements for pharmacists, discounting the professional education and training provided by schools and colleges of pharmacy and ignoring the professional responsibilities of pharmacists themselves.

Pharmacy is a profession. Professionals self-regulate their provision of care to those things they know they are competent to provide. I'd personally never, as a pharmacist, provide oncology medications or services because I know full well that I'm incompetent in oncology—this should be left to pharmacists who are specially trained and board certified.

We've unintentionally said to the world that we don't trust ourselves to self-regulate. As a pharmacist, I find it insulting—and in my discussions with pharmacists across the country, I'm not alone in this feeling.

State boards of pharmacy and state pharmacy associations: it's time to unwind the mess that has been created over 30 years and start treating pharmacists as true professionals. Let's stop placing extra educational requirements on pharmacists going forward. If a pharmacist engages in a practice that is outside of his or her knowledge, leading to harm of a patient, then the pharmacist should be accountable for that irresponsible action. And if they want to provide a service for which they feel they need more training, a plethora of options exist in the marketplace to avail themselves of that training. That's how it works in medicine, nursing, dentistry, and all other professions. And that's how it should work in pharmacy, too.

For every pharmacist. For all of pharmacy. ■

## NEW DRUGS

### RESMETIROM
**(Rezdiffra—Madrigal Pharmaceuticals)**

**Drug class:** Rezdiffra is a thyroid hormone receptor-beta (THR-beta) agonist.

**Indication:** Rezdiffra is indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). Avoid use of Rezdiffra in patients with decompensated cirrhosis.

**Recommended dosage and administration:** The recommended dosage of Rezdiffra is based on actual body weight. For patients weighing <100 kg, the recommended dosage is 80 mg orally once daily. For patients weighing >100 kg, the recommended dosage is 100 mg orally once daily. Administer Rezdiffra with or without food.

**Common adverse effects:** The most common adverse reactions with Rezdiffra are diarrhea, nausea, pruritus, vomiting, constipation, abdominal pain, and dizziness.


**Warnings and precautions:** Monitor patients during treatment with Rezdiffra for elevations in liver tests and for the development of liver-related adverse reactions. Discontinue Rezdiffra and continue to monitor the patient if hepatotoxicity is suspected.

Cholelithiasis and cholecystitis were observed more often in patients treated with Rezdiffra. If cholelithiasis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated. If an acute gallbladder event such as acute cholecystitis is suspected, interrupt Rezdiffra treatment until the event is resolved. Concomitant use with strong or moderate CYP2C8 inhibitors or OATP1B1 and OATP1B3 inhibitors is not recommended. If used concomitantly with atorvastatin, pravastatin, rosuvastatin, or simvastatin, limit the daily dosage of the statin as recommended. If used concomitantly with CYP2C8 substrates, monitor patients more frequently for substrate-related adverse reactions. Avoid use of Rezdiffra in patients with moderate to severe hepatic impairment.

### APROCITENTAN
**(Tryvio—Idorsia)**

**Drug class:** Tryvio is an endothelin receptor antagonist.

**Indication:** Tryvio is indicated for the treatment of hypertension in combination with other antihypertensive drugs, to lower BP in adult patients who are not adequately controlled on other drugs. Lowering BP reduces the risk of fatal and nonfatal CV events, primarily strokes and myocardial infarctions.

**Recommended dosage and administration:** The recommended dosage of Tryvio is 12.5 mg orally once daily with or without food.

**Common adverse effects:** The most common adverse reactions are edema and anemia.

**Boxed warning:** Tryvio can cause major birth defects if used by pregnant patients and is contraindicated during pregnancy. Exclude pregnancy prior to initiation of treatment, monthly during treatment, and for 1 month after stopping Tryvio. Use acceptable contraception prior to initiation of treatment, during treatment, and for 1 month after stopping Tryvio. Tryvio is only available through a restricted distribution program called the Tryvio REMS.

**Other warnings and precautions:** Tryvio is contraindicated in pregnancy and hypersensitivity. Endothelin receptor antagonists can cause hepatotoxicity and liver failure. Measure serum aminotransferase levels and total bilirubin prior to initiation of treatment and repeat periodically during treatment and as clinically indicated. Fluid retention may require intervention. Decreases in hemoglobin and decreased sperm counts may occur. Patients should be advised not to breastfeed.

### GIVINOSTAT
**(Duvyzat—Italfarmaco)**

**Drug class:** Duvyzat is a histone deacetylase inhibitor.

**Indication:** Duvyzat is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 6 years and older.

**Recommended dosage and administration:** Obtain and evaluate baseline platelet counts and triglycerides prior to initiation of Duvyzat. Do not initiate Duvyzat in patients with a platelet count <150 x $10^9$/L.

The dose of Duvyzat is based on the patient's body weight. Administer orally twice daily with food. Dosage modifications may be needed for decreased platelet counts, diarrhea, increased triglycerides or QTc prolongation.


**Common adverse effects:** The most common adverse reactions are diarrhea, abdominal pain, thrombocytopenia, nausea/vomiting, hypertriglyceridemia, and pyrexia.

**Warnings and precautions:** Duvyzat can cause dose-related thrombocytopenia and other signs of myelosuppression, including anemia and neutropenia. Monitor platelets, as dosage adjustment or discontinuation may be needed.

An increase in triglycerides can occur and dosage modification or discontinuation may be needed. Adjust dosage if moderate or severe diarrhea occurs. Antiemetics or antidiarrheal

medications may be considered during treatment with Duvyzat. Discontinue if the symptoms persist. Avoid use of Duvyzat in patients who are at an increased risk for ventricular arrhythmias.

Closely monitor when Duvyzat is used in combination with an oral CYP3A4 sensitive substrate or a sensitive substrate of the OCT2 transporter, for which a small change in substrate plasma concentration may lead to serious toxicities.

Avoid concomitant use with other drugs that prolong the QTc interval and monitor ECG if concomitant use cannot be avoided. Based on animal data, use in pregnancy may cause fetal harm. In hepatic impairment, exposure to givinostat is expected to be increased.

## NEW DOSAGE FORMS

### RILPIVIRINE
**(Edurant PED—Janssen)**

**Drug class:** Edurant PED is an HIV-1 specific, non-nucleoside reverse transcriptase inhibitor (NNRTI).

**Indication:** Edurant PED is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-naive patients 2 years and older and weighing at least 14 kg with HIV-1 RNA ≥100,000 copies/mL.

**Recommended dosage and administration:** The recommended dosage of Edurant PED is based on body weight for pediatric patients 2 years and older and weighing ≥14 kg to ≤25 kg. Edurant PED tablets must be dispersed in drinking water and taken with a meal.

**Common adverse effects:** The most common adverse reactions to Edurant PED were depressive disorders, headache, insomnia, and rash.

**Warnings and precautions:** Coadministration of Edurant PED is contraindicated with drugs for which significant decreases in rilpivirine plasma concentrations may occur, which may result in loss of virologic response and possible resistance and cross-resistance.

Severe skin and hypersensitivity reactions have been reported. Immediately discontinue treatment if hypersensitivity or rash with systemic symptoms or elevations in hepatic serum biochemistries develop, and closely monitor clinical status including hepatic serum biochemistries. Hepatic adverse events have been reported in patients with underlying liver disease, including hepatitis B or C virus coinfection, or in patients with elevated baseline transaminases. Monitor liver function tests before and during treatment with Edurant PED in patients with underlying hepatic disease or marked elevations in transaminase.

Also consider monitoring liver functions tests in patients without pre-existing hepatic dysfunction or other risk factors. Severe depressive disorders have been reported. Immediate medical evaluation is recommended for severe depressive disorders. Patients may develop immune reconstitution syndrome. Consider alternatives to Edurant PED when it would be coadministered with drugs with a known risk of torsade de pointes. Edurant PED should not be used in combination with NNRTIs.

Coadministration with drugs that induce or inhibit CYP3A may affect the plasma concentrations of rilpivirine. Coadministration with drugs that increase gastric pH may decrease plasma concentrations of rilpivirine. Total rilpivirine exposures were generally lower during pregnancy compared to the postpartum period.

## NEW COMBINATIONS

### MACITENTAN AND TADALAFIL
**(Opsynvi—Actelion)**

**Drug class:** Opsynvi is a combination of macitentan, an endothelin receptor antagonist, and tadalafil, a phosphodiesterase 5 (PDE5) inhibitor.

**Indication:** Opsynvi is indicated for chronic treatment of pulmonary arterial hypertension in adult patients of WHO functional class II–III. Macitentan reduces the risk of clinical worsening events and hospitalization. Tadalafil improves exercise ability.

**Recommended dosage and administration:** The recommended dosage is one 10 mg/20 mg or 10 mg/40 mg tablet taken orally once daily with or without food.

**Common adverse effects:** The most common adverse reactions are edema, anemia, and headache/migraine.

**Other warnings and precautions:** Opsynvi is contraindicated in pregnancy, hypersensitivity, concomitant organic nitrates, and concomitant guanylate cyclase stimulators.

Endothelin receptor antagonists cause hepatotoxicity and liver failure. Obtain baseline liver enzymes and monitor as clinically indicated. Vasodilatory effects may cause hypotension in susceptible patients. Decreases in hemoglobin may occur. Worsening pulmonary veno-occlusive disease may occur so if pulmonary edema is confirmed, discontinue treatment.

Sudden loss of vision could be a sign of nonarteritic ischemic optic neuropathy and may be permanent. Cases of sudden decrease or loss of hearing have been reported in patients taking tadalafil. Fluid retention may require intervention. Avoid use with other PDE5 inhbitors. Decreases in sperm count have been observed in patients taking endothelin receptor antagonists. Advise patients to seek emergency treatment if an erection lasts more than 4 hours.

Avoid concomitant use with strong CYP3A4 inducers and inhibitors and moderate dual or combined CYP3A4 and CYP2C9 inhibitors. Advise patients not to breastfeed during treatment. Avoid use in patients with creatinine clearance of 15 mL/min to 29 mL/min. Do not initiate in patients with severe hepatic impairment. ■

**Also in this issue**
FDA approves Xolair, the first medication indicated to help reduce allergic reactions to foods (page 18)

# UTIs: Common and treatable

Mary Warner

Urinary tract infections are among the most common bacterial infections, accounting for almost 9 million ambulatory care visits per year. Women are more likely to develop a UTI than men, and one in three women will develop a UTI requiring treatment before they are 24 years old. Although antibiotics are necessary to resolve the infection, nonprescription medications can help resolve symptoms while the antibiotics do their work.

Nonprescription UTI relief medications are intended to address the symptoms of UTIs while antibiotics are used to treat the underlying infection.

## Risk factors and prevention

As mentioned above, UTIs are more common in women than in men because of anatomic differences; women increase their risk of developing a UTI by wiping from back to front after urination. Additional risk factors in women include diaphragm use, sexual intercourse, a history of UTIs, maternal history of UTI, and being postmenopausal. In men, benign prostatic hypertrophy can increase the risk of developing a UTI. Conditions that prevent complete emptying of the bladder can also contribute to development of a UTI.

Increased fluid intake and complete voiding of the bladder have been suggested as ways to prevent UTIs, but research has not proven these routines to be effective. Increased fluid intake may dilute the bacteria in the urinary tract and increase voiding frequency, but it does nothing to prevent a UTI from developing.

## What about cranberry juice?

Cranberry juice has long been touted as a way to both prevent and treat UTIs because it contains proanthocyanidins (PACs), substances that can prevent bacteria from sticking to the walls of the bladder and may prevent infections. However, the authors of a Cochrane review published on November 10, 2023, point out the there is no established regimen for PAC dosage and that there is no formal regulation of cranberry products by health care authorities.

The authors of the review analyzed the results of 50 randomized controlled trials involving almost 9,000 patients that compared the occurrence of UTIs in people taking a cranberry product with those taking a placebo or receiving no treatment. They found that taking cranberries as a juice, tablet, or capsule reduced the number of UTIs in women with recurrent UTIs, in children with UTIs, and in people susceptible to UTIs following an intervention such as bladder radiotherapy. However, UTI occurrence did not appear to be reduced in older patients, in adults with neuromuscular bladder dysfunction and incomplete bladder emptying, or in pregnant women.

Few patients reported adverse effects, with the most common being stomach pain. The researchers concluded that further assessment is required to clarify further which patient populations could benefit from cranberry products.

## Treating the symptoms

The most common symptoms of a UTI are a strong, frequent urge to urinate; pain or a burning sensation during urination; cramping in the lower back or sides; foul-smelling or cloudy urine; and rectal pain (in men) or pelvic pain (in women).

Nonprescription UTI relief medications are intended to address the symptoms of UTIs while antibiotics are used to treat the underlying infection.

Most of these OTC products contain phenazopyridine hydrochloride, which may alleviate the burning, pain, and constant feeling of having to urinate. Because phenazopyridine hydrochloride is a dye, it usually causes urine to turn a harmless bright yellow or dark orange color. Some kits also contain UTI test strips, but it's important to note that these do not detect the presence of bacteria, but only measure nitrate, pH, and leukocyte levels, which could indicate a UTI.

## What to tell your patients

Ensure that patients understand that nonprescription UTI relief products only relieve the pain and do not treat bacterial infections, and that prescription antibiotic medications are required to eliminate the bacteria, often *E. coli*, that cause UTIs. Advise patients who suspect a UTI to see their physician as soon as possible for a definitive urine test and appropriate antibiotic treatment. Nonprescription relief products can be used to manage symptoms until the infection has been eliminated. ■

# Biotin: Boon or bunk?

Mickie Cathers

Biotin has been at the top of supplement charts for years, promoted as being beneficial for shiny, thick hair; strong and fast-growing nails; and healthy, radiant skin. Some biotin dietary supplements also claim to support energy, metabolism, and the nervous system. But is biotin clinically efficacious or just a trend?

## Background

Biotin (vitamin $B_7$ or vitamin H) is a water-soluble essential nutrient found in foods such as beef liver, eggs, fish, seeds, nuts, and some vegetables such as sweet potatoes. Biotin acts as an essential cofactor for multiple carboxylases involved in the metabolism of amino acids, fatty acids, and glucose. Biotin also plays key roles in histone modifications, cell signaling, and epigenetic regulation. Most biotin in foods is bound to protein, though some dietary biotin is in the free form. Free biotin is absorbed in the small intestine while most biotin is stored in the liver. Excess biotin is excreted in the urine.

Biotin deficiency may cause brittle nails, thinning of hair, and a red scaly rash on the face. However, biotin deficiency is rare and severe biotin deficiency has never been reported. While biotin is necessary for normal body function, most people get the biotin they need from a healthy and balanced diet.

Supplements may help pregnant women who develop marginal biotin deficiency despite normal biotin intake, some smokers, and some patients with alcohol use disorder. However, there is insufficient data to support or recommend biotin supplementation.

## Is there a benefit?

Despite its reputation, there is limited research to support biotin supplementation to improve hair, skin, and nail health. Reviews have revealed underpowered studies as well as studies that didn't include a placebo group or neglected to include a baseline biotin status of study participants. Differences in hair and nail growth were not statistically significant in these studies. Only case reports are available to support claims that biotin supplements promote hair health, and these reports were only in children.

There have been no clinical trials or randomized controlled trials to study biotin's effect on alopecia, hair quality, or hair quantity in human subjects. There are no recommendations in the literature, or from FDA or NIH, for biotin supplementation due to this lack of evidence.

## Dosage and availability

Biotin supplements are available online and on store shelves as chewable tablets, capsules, softgels, gummies, liquid drops, and powders. These products offer biotin alone or in combination with other B-complex vitamins or other multivitamin and multimineral products, such as magnesium, collagen, or keratin. Oral biotin's absorption rate is 100%, even in doses of up to 20 mg/day. Biotin is also available in creams and other cosmetic products, which typically contain up to 0.6% biotin, as well as intravenously through a health care provider.

Available data are insufficient for determining recommended dosages. FDA doesn't recommend daily biotin supplementation, except for breastfeeding or pregnant patients, who are recommended to take from 5 µg/day to 35 µg/day. NIH suggests an adequate daily intake for adults 19 years and older of 30 µg/day. For children from birth to 18 years, the range is 5 µg/day to 25 µg/day.

## What to tell your patients

Though supplementation remains unnecessary in healthy individuals, biotin is generally considered safe, even for children and pregnant and breastfeeding patients. Adverse effects of ingesting too much biotin could include nausea or upset stomach, though this is uncommon. As biotin is water-soluble, excess is excreted in the urine. However, biotin may interfere with the results of some blood lab tests and hormone assays, and can interact with certain medications, including anticonvulsants. Advise patients to mention their supplements when talking with their health care provider. ■


# Using Xolair to reduce allergic reactions to foods

Lauren Howell, PharmD

On February 16, 2024, FDA approved the first medication indicated to help reduce allergic reactions to more than one type of food after accidental exposure. Xolair (omalizumab—Genentech) injection is approved for the reduction of type I allergic reactions, including reducing the risk of anaphylaxis that may occur with accidental exposure to one or more foods in adults and children 1 year or older.

While this breakthrough for individuals with food allergies does not mean that they can consume allergens freely, it does mean that repeated use of the medication can help to reduce allergic reactions if accidental exposure occurs. Xolair was previously approved to treat allergic asthma, chronic spontaneous urticaria, and chronic rhinosinusitis in certain patients, but this new indication provides a treatment option for those with food allergies, for which there is currently no cure.

## Recommended dosage and administration

The recommended dosage of Xolair is 75 mg to 600 mg administered subcutaneously every 2 or 4 weeks. The exact dose and dosing frequency should be determined based on a serum total immunoglobulin E (IgE) level measured before the start of treatment and body weight. If significant changes to body weight occur during treatment, the dose should be adjusted.

During treatment, total IgE levels are elevated and can remain elevated for up to 1 year after Xolair is discontinued. Because of this, retesting of serum IgE levels during treatment should not be used to adjust the dose that the patient receives.

If there is an interruption in treatment that lasts less than 1 year, the dose given should be based on the serum IgE levels that were obtained at the initial dose determination. If treatment is interrupted for 1 year or longer, total serum IgE levels should be retested and a new dosing determination should be made.

Xolair is indicated to be used in conjunction with food allergen avoidance and is not intended to replace it. It is also not indicated for the emergency treatment of allergic reactions, including anaphylaxis.

## Adverse effects, warnings, and precautions

Xolair carries a boxed warning for anaphylaxis presenting as bronchospasm, hypotension, syncope, urticaria, or angioedema of the throat or tongue. This anaphylaxis can occur after the first dose of Xolair but may also occur 1 year after beginning regularly administered treatment.

Due to this risk, Xolair should be administered in a health care setting and patients should be closely observed after administration. Once therapy has been safely established, the health care provider may determine whether self-administration by the patient or caregiver is appropriate based on assessment of risk for anaphylaxis and mitigation strategies.

The most common adverse reactions in patients receiving Xolair for treatment of IgE-mediated food allergy are pyrexia and injection site reactions. Malignancies have been observed in clinical studies. Corticosteroids should not be abruptly discontinued upon initiation of Xolair therapy.

Be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and neuropathy, especially when oral corticosteroid dose reduction occurs. Stop Xolair if patients develop signs and symptoms such as serum sickness, including fever, arthralgia, and rash.

## Clinical studies

The safety and efficacy of Xolair were evaluated in a multicenter, randomized, double-blind, placebo-controlled food allergy trial that included 168 patients ranging between 1 year and 56 years old. These patients were allergic to peanuts and at least two other foods, including milk, egg, wheat, cashew, hazelnut, or walnut, and experienced dose-limiting symptoms (e.g., moderate to severe skin, respiratory, or GI symptoms) to a single dose of up to 100 mg of peanut protein and up to 300 mg protein of each of the other two foods. Patients with a history of severe anaphylaxis were not included in the study.

Patients were randomized to either receive Xolair or placebo for 16 to 20 weeks. The primary efficacy endpoint was the percentage of patients who were able to consume a single dose of at least 600 mg of peanut protein without dose-limiting symptoms (68% in the Xolair treatment group and 5% in the placebo group).

Similar results were seen when patients were exposed to a single dose of at least 100 mg of cashew, milk, or egg protein. Xolair treatment led to statistically higher response rates than placebo for all three foods. ■

# COVID-19 vaccine safety: Biggest microscope yet finds little new

John D. Grabenstein, RPh, PhD, FAPhA

Results of a COVID-19 vaccine safety study that included over 99 million patients from eight countries were released in February 2024.

News headlines were generally accurate, but the sample below shows how some titles were misleading:

- "Largest COVID vaccine study ever reveals the actual health risks you face"
- "Covid-19: Two rare vaccine side effects detected in large global study"
- "Largest multicountry COVID study links vaccines to potential adverse effects"
- "Study of 99 million COVID-vaccinated people finds links to brain, heart problems"
- "Despite sensational reports, COVID-19 vaccine safety outweighs risks"
- "Covid vaccines linked to small increase in heart and brain disorders, study finds—but risk from infection is far higher"

The remarkably large number of vaccinees in the GVDN paper allowed the researchers to apply one of the biggest "microscopes" yet to assess very rare events.

What most of these headlines lack is perspective. Most of the links to adverse effects reported in these news items were for vaccines distributed outside the United States, and the new connections discovered and relevant to the United States are not confirmed cause-and-effect relationships.

All medications carry risks. But how can we ignore the benefits? COVID-19 vaccinations prevented more than 18 million hospitalizations and 3 million deaths in the United States alone, and even more globally.

So, as pharmacists engage with their patients, it is helpful to keep in mind these details about the 99-million-vaccinee study specifically and the U.S. vaccine safety surveillance program in general.

## COVID-19 vaccines and the Global Vaccine Data Network study

To complete the study, the Global Vaccine Data Network (GVDN) compiled data from 10 sites across eight countries (not including the United States), comparing observed and expected rates of 13 adverse events among 99,068,901 COVID-19 vaccine recipients.

This study confirmed the rare association between mRNA COVID-19 vaccines and myocarditis that U.S. officials have been educating clinicians and the public about since 2021. GVDN researchers also showed there is no link between mRNA vaccination and Guillain-Barré syndrome, transverse myelitis, Bell's palsy, convulsions, febrile seizures, various forms of thrombosis, or pulmonary embolism.

A signal for risk of acute disseminated encephalomyelitis that requires further study was identified. Seven cases were found after 10 million first doses of Moderna's mRNA vaccine in these databases, whereas two cases were expected. Other studies—including a companion study —did not find such an association, so this remains a signal rather than a confirmed risk.

The remarkably large number of vaccinees in the GVDN paper allowed the researchers to apply one of the biggest "microscopes" yet to assess very rare events. The other safety signals identified are so very rare that even if they turn out to have a cause-and-effect relationship, they would need to be compared to the risks of driving across town to be vaccinated.

## The U.S. Vaccine Safety Surveillance Program

CDC coordinates an overlapping set of vaccine safety surveillance programs, partnering with other government agencies and multiple universities and health systems. The surveillance program encompasses more than a dozen projects and fulfills an important public responsibility: to keep eyes and ears open for unexpected findings. Where any one program has a limitation, another program among the set has a corresponding strength to bear.

CDC and its partners have presented their safety findings at each public meeting of ACIP since late 2020—at least 30 meetings. That scrutiny assesses more than 700 million COVID-19 vaccinations administered in the United States since December 2020.

The common adverse events, those happening at rates of 1 per 100 up to 1 per 10,000 vaccinations, attributable to COVID-19 vaccination are very well understood. Even so, the nation's eyes and ears remain open to learn about even rarer events or events that happen in subsets of the population. All in all, vaccines are medications that carry risks and benefits. COVID-19 vaccination remains the best, most reliable way to prevent a serious COVID-19 infection, hospitalization, or death.

## Perspective

Four years after the pandemic started, several thousand Americans continue to be hospitalized each week due to COVID-19 infection. Many of those hospitalizations could be prevented by wider use of COVID-19 vaccines.

The risks from vaccination pale in comparison to the risk from COVID-19. Pharmacists and their teammates are the leading COVID-19 vaccination providers in America.

Remember to read the full details, rather than assuming the headline tells the whole story.

References avaliable online at pharmacytoday.org. ■

# Balancing act: Gabapentinoids and exacerbation risk in COPD

Aiya Almogaber, PharmD

Gabapentinoids, such as gabapentin and pregabalin, are commonly used in the management of epilepsy and neuropathic pain. However, these medications have recently come under scrutiny due to potential respiratory adverse effects, particularly in patients with COPD, which are characterized by progressive airflow limitation and recurrent exacerbations that impact a person's quality of life.

In a study published in January 2024 in the *Annals of Internal Medicine,* researchers shined a light on the potential risks, such as severe exacerbations and respiratory failure, of gabapentinoids for patients with COPD. The study emerged following warnings issued by health authorities in North America and Europe regarding these serious respiratory complications.

"These warnings were based mainly on case reports, and there was a lack of large population-based studies on this topic, which led us to conduct this study assessing the association between gabapentinoid use and severe exacerbation of COPD [hospitalization]," said the study authors.

The findings offer valuable insights for pharmacists and other health care professionals and can equip them with critical data to inform their clinical decision making.

## The study

By analyzing insurance records from the Régie de l'assurance maladie du Québec, Canada, Rahman and colleagues focused on a specific cohort: COPD patients aged 55 years and older who had been prescribed multiple respiratory medications between 1994 and 2015. Researchers compared those who started gabapentinoid therapy for conditions such as epilepsy, neuropathic pain, or chronic pain, with nonusers of gabapentinoids. Individuals were matched based on COPD duration, age, sex, and a nuanced time-conditional propensity score.

The primary outcome measured was severe COPD exacerbation requiring hospitalization, with secondary outcomes including moderate or severe exacerbation and respiratory failure.

The findings indicate that gabapentinoid use was associated with an increased risk of severe COPD exacerbation across all indications. Specifically, hazard ratios revealed a heightened risk ranging from 1.35 to 1.58, depending on the indication, with an overall hazard ratio of 1.39. The authors said that these findings largely aligned with their initial hypothesis, noting that they expected to identify an increased risk of severe exacerbations associated with gabapentinoid use. This underscores the importance of cautious gabapentinoid prescribing in this patient population.

The results are consistent with prior evidence from case reports, pharmacovigilance databases, and clinical studies highlighting the respiratory risks associated with gabapentinoids. Results were also consistent with existing warnings for cautious consideration when prescribing medications in this drug class.

## Takeaways

Health care practitioners who are involved in managing patients diagnosed with COPD should thoroughly assess patients, take advantage of educational initiatives, and work collaboratively to effectively navigate the challenges associated with treating concurrent conditions in this vulnerable population.

As noted by the authors, these results highlight the importance of coordination among a patient's circle of care, as the provider managing COPD may differ from the provider prescribing gabapentinoids.

Pharmacists are uniquely positioned to care for COPD patients, too, often serving as the final point of contact.

The first implication for pharmacy practice is clinical vigilance. When dispensing gabapentinoid drugs to patients with COPD, it is important to be mindful of the potential for severe respiratory exacerbations, among other potential adverse effects. Counseling and medication therapy management, areas in which pharmacists are adept, can help mitigate these risks.

Regular medication reviews offer an opportunity to assess the appropriateness of gabapentinoid use in patients with COPD. Pharmacists can collaborate with prescribers to consider or recommend alternative pain management strategies when necessary.

The decision to initiate or continue gabapentinoid therapy in COPD patients should involve a thorough risk–benefit analysis, taking into account the severity of pain or epilepsy and the patient's overall respiratory status.

Patients should also be encouraged to independently monitor and report adverse drug reactions, including severe COPD exacerbations associated with gabapentinoid use. Symptoms may include an increase in the amount, thickness, or color of mucus or sputum; a noticeable change in shortness of breath; an increase in the severity of coughing; changes in the color or consistency of phlegm; new or worsening wheezing when breathing; chest tightness or discomfort; increased fatigue; difficulty sleeping due to breathing problems; or swelling in the ankles, feet, or legs.

Advise patients that recognizing and responding to these symptoms quickly can prevent further deterioration of their condition, aid in the accumulation of evidence that can guide future prescribing, and contribute to overall patient safety. ■

# Weight plays a role in pediatric prescriptions

Elizabeth Briand

When it comes to dispensing medications for infants and children, even the smallest of miscalculations could have potentially serious consequences. Traditionally, though, one piece of information—the weight of pediatric patients—has not been provided by prescribers, leaving it up to pharmacists to check weights or provide safe dosing guidelines for parents and caregivers.

Providing weight "hasn't been the standard of practice," said Sarah Oprinovich, PharmD, from the University of Missouri-Kansas City School of Pharmacy.

Oprinovich coauthored a study on pediatric weight-based antibiotic dosing published last year in *JAPhA*. The study found that of 115 prescriptions evaluated, 45 were missing a patient's weight, diagnosis code, or both, and of the remaining 70 considered optimal—defined as including patient weight and diagnosis code—42 were prescribed outside of guideline-recommended dosing, with low dosing the most common result.

"The data sent to the pharmacy are the least amount of data necessary," said Jake Galdo, PharmD, managing network facilitator for CPESN Health Equity. "Some management systems have no ability to document the weight of a child. Others do."

While conducting the study, Oprinovich and her fellow researchers discovered that software parameters played a significant role in the absence of a patient's weight.

"It has to do with settings in e-prescribing [systems at] the pharmacy receiving the prescription," said Oprinovich. "When we ran the reports to see where weights were included, we found that they were being transferred [to the pharmacist] in the background of files, usually with the vitals. They were there; they just weren't in a conspicuous spot."

## The value of knowing weights

Patient weight is of greater concern with certain medications. These include baclofen, especially in an oral suspension, or any other medications that can possibly be compounded, according to Brenda Denson, PharmD, pharmacy educator at Children's of Alabama.

"There are so many strengths of compounded medications. The weight [of a patient] is so important in checking the accuracy of the doses," said Denson.

Some medications, according to Denson, should not be dispensed at all without knowing the patient's weight. These include sedating agents, medications with muscle relaxing potential, and some medications for seizures.

"There are some medications [for which] it's really important to know the weight, like heart failure medications, and those are going to get your attention," said Oprinovich. "You'll spend a bit more time on medications like that. You'll be more likely to call and check the weight, but that takes extra time. Having the weight [in hand] would save all of that."

Weight can also play an important role in how well antibiotics work. Underdosing can often lead to decreased effectiveness of antibiotics.

"If [the child] is on their third antibiotic, that means it didn't treat it," said Galdo, who is also CEO of Seguridad, which produces safety scorecards for community pharmacies.

## Tracking down the details

Galdo suggests that pharmacists actively pursue getting a child's weight. "I'm a health care provider and can have a scale in my pharmacy and collect weight," he said. "When someone comes in to get a kid's prescription, I'll ask them if they know their child's weight. If they don't, then I'll say this dose is between weights of this and that, so please check when you get home. 'If [they're] not between those weights, then please call me.'"

But many pharmacists, especially in community practice, may not have the ability to get a child's weight.

Ultimately, the creation of software systems that would make it easier to see embedded data such as weight could save pharmacists time and ensure accuracy.

If weights were easier to access, it would take pharmacists less time to verify dosing. "It needs to be an easy system—you don't want to have to click five screens to get the information," said Oprinovich. "You just want it to be available."

Having weight and other key details in hand could be important factors in safety as well as quality. "Our minimum standard is to make sure it's the right dose and equip ourselves to make that happen," said Galdo. ■

# Ready or not, psychedelic medicine is coming to market

Sonya Collins

In February, FDA accepted Lykos Therapeutics' new drug application (NDA) for midomafetamine (MDMA) capsules, used in combination with psychotherapy, for the treatment of PTSD. If the treatment is approved, a decision that could come as soon as August 2024, it will be the first in what is expected to be a growing number of FDA-approved psychedelic-assisted therapies.

Clinical trials of psilocybin are underway as well. If the trials are successful, this psychedelic agent found in magic mushrooms could see FDA approval for the treatment of severe depression in the next few years.

Evidence for these once-illicit drugs is part of a growing body of research that supports their benefits in several mental health conditions. The question is no longer if psychedelic medicine will one day be among the treatment options for mental health conditions, but rather when.

Patients are ready for these new drugs, too—that is, if they aren't using them already. Two-thirds of Americans support regulated, therapeutic use of psychedelics, according to an online survey conducted by UC Berkeley Center for the Science of Psychedelics. An estimated one in four Americans has tried at least one psychedelic drug in their lifetime, another survey found. And that number seems to be rapidly climbing; the number of Americans over 12 years old who report using hallucinogens has doubled in the last 10 years.

"Upon the FDA approval of these compounds, we need pharmacists to be a part of that discussion, a part of the care framework, so that we can ensure that access, safety, accountability—all the things that pharmacists are already providing now—can be translated into psychedelic care systems," said Sa'ed Al-Olimat, PharmD, cofounder of the Psychedelic Pharmacists Association.

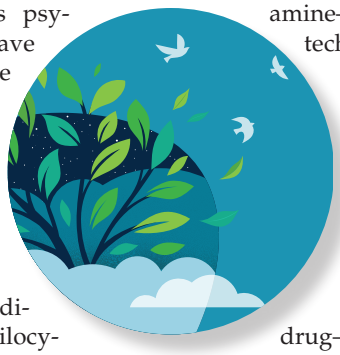
Lykos Therapeutics' NDA includes results from two randomized, double-blind, placebo-controlled Phase 3 studies, MAPP1 and MAPP2, published in *Nature Medicine* in 2023. In both trials, patients who received MDMA plus psychotherapy saw significantly more improvement in PTSD symptom severity and functional ability than those on a placebo plus psychotherapy.

As for psilocybin, in a 2021 head-to-head comparison of the psychedelic agent and SSRI escitalopram plus psychotherapy published in *NEJM*, the

Evidence for these once-illicit drugs is part of a growing body of research that supports their benefits in several mental health conditions.

psychedelic was not superior to the conventional antidepressant. But subsequent trials have shown it relieves depression compared to placebo. Numerous other trials are currently underway to further measure psilocybin's benefits in treatment-resistant depression.

MDMA and psilocybin are the psychedelic drugs closest to earning FDA approval for mental health conditions and coming to the U.S. market in the near term. But they are just two among numerous psychedelic agents that have some degree of evidence to support their benefits for mental health conditions such as treatment-resistant depression, PTSD, OCD, eating disorders, and SUDs.



Psychedelics in addition to MDMA and psilocybin that have been investigated for these benefits include lysergic acid diethylamide (LSD); N,N-dimethyltryptamine (DMT); ayahuasca, a psychoactive brew originating from the Amazon basin that contains both DMT and naturally occurring MAOIs; 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT); and mescaline (3,4,5-trimethoxyphenethylamine), the psychedelic agent found in the peyote plant.

## Psychedelic-assisted psychotherapy

Many of the benefits of these drugs have been seen in the context of psychedelic-assisted therapy. That is, the drugs are seen to enhance the effects of psychotherapy and achieve results that neither the drug nor psychotherapy alone could.

"Psychedelics act on specific serotonin receptors to increase glutamatergic activity in the brain," Al-Olimat said. This, researchers believe, fosters new neuronal connections in the brain. When normal brain functioning is disrupted, psychedelics seem to repair or reset these broken networks.

"What this allows," Al-Olimat said, "is for novel insights to take place, so enhanced perception, enhanced perspective. These experiences that come from the macrodose experience are insights that patients can take away from, reflect on, and integrate into their daily lives for habit change."

Psychedelics' actions in the brain allow patients to make meaning out of what they see or feel during the dissociative, psychedelic experience, and facilitate meaningful insights and changes in talk therapy.

Some physicians are using ketamine—a dissociative, but not technically a psychedelic drug—in the same way: as an adjuvant to psychotherapy. Depending on the protocol, patients may receive a ketamine infusion in a physician's office or sublingual lozenges under video supervision at home on what's called their "dose day," and follow up the dose on another day with what's called "integration"—a talk therapy session in which the patient unpacks and makes sense of the psychedelic experience and its applications to their recovery from their mental health condition.

The psychedelic-assisted therapy model is predicated on the idea that both the neuroplastic and psychedelic effects of the drug are needed to achieve the mental health benefits. Depending on the drug and the treatment protocol, this model may require a time-consuming medication washout, hours of preparation with a therapist, multiple dose days during which a dissociative experience takes place and may last several hours, and hours of integration therapy after dose days.

Some research underway aims to isolate compounds from psychedelic agents that would cause the neuroplastic effects without the psychedelic trip to determine whether it would be beneficial in the treatment of mental illnesses.

A multi-institutional team of researchers from UCSF, Yale, and Duke has isolated compounds from the African medicinal plant ibogaine that may act on serotonin in the same way as the natural psychedelic does—to treat depression and SUDs—but without its many dangerous adverse effects that can include heart arrhythmias.

"Not everyone has the time or luxury to do hours and hours of preparation, followed by a 4- to 6- or 8-hour experience, one to three times, followed by integration afterwards," Al-Olimat said. Others may not meet inclusion criteria for psychedelics due to health risks.

"If those patients are able to take a pill to get that neuronal growth without having a full-blown mystical experience that should be an option," Al-Olimat said.

> The entrance of psychedelics onto the mainstream prescription drug market will mark a major paradigm shift.

## Paradigm shift

The entrance of psychedelics onto the mainstream prescription drug market will mark a major paradigm shift as the psychoactive substances in these drugs have been illegal until now. With this shift, pharmacists may need to take stock of their own biases.

"If you had no idea it was a psychedelic, and you read the literature," Al-Olimat said, "you'd say, 'Wow! One to three doses of this novel compound and we see alleviation of symptoms of depression, anxiety, PTSD, and other potential indications. Why aren't we doing more research on this? Why aren't we talking about this?'"

Pharmacists have likely encountered people—many of whom have suffered for years on traditional antidepressants with no relief—who

are already accessing psychedelics for mental health purposes or seriously considering it. Besides through clinical trials, patients may be accessing psychedelics through wellness retreats or religious ceremonies both in the United States and abroad.

"These are viable treatment options for people either now or in the future," said Benjamin Malcolm, PharmD, founder of Spirit Pharmacist, an online service through which he provides consulting and education on psychedelics. "The train has left the station."

For this reason, pharmacists may prepare themselves to provide objective answers to patients' questions about psychedelics.

"People deserve to have all the information about all the options when they make decisions about their health," Malcolm said.

It's in the name of providing people the information they deserve that Malcolm has found a role for himself as a pharmacist in the field of psychedelic medicine. Through video chats, he provides psychedelic education and psychopharmacological consulting. His clients range from individuals who have used or are interested in using psychedelics and have questions, to providers such as psychiatrists designing clinical trials, psychedelic-assisted therapy facilitators, organizations, and others.

Malcolm knows from his experience consulting patients who are curious about the potential benefits of psychedelics that "In those 30 seconds or 1 minute at the pharmacy counter, if you can just let the person know that they are not crazy or criminal for thinking about this, that should be the goal."

To further normalize and destigmatize the encounter, pharmacists could prepare a printed handout including the potential benefits and risks of psychedelics in the treatment of mental health conditions and a list of resources for patients to consult.

Resources to consider include:

- MAPS.org: The Multidisciplinary Association for Psychedelic Studies offers articles, resources, and downloadable exercises.
- The Fireside Project provides telephone-based peer support during or after a psychedelic experience.
- Information about some of the few pharmacists who provide online education and consultation on psychedelic medicine, such as Malcolm at SpiritPharmacist.com and Emily Kulpa, PharmD, at DrEmilyKulpa.com.

## Roles for pharmacists

Patients are already accessing psychedelics for mental health care with or without a pharmacist's involvement.

Pharmacists may prepare themselves to provide objective answers to patients' questions about psychedelics.

Malcolm stresses that not every community pharmacist needs to become an expert in psychedelic medicine. They just need to be prepared to listen and respond without judgment.

"It would be best to say something along the lines of, 'I'm not an expert in this area, but I hear there could be some promise with psychedelics, but I also know you have to be careful about who receives them and under what circumstances'," he said.

"The psychedelics space is rapidly evolving and no one's talking about pharmacists," Al-Olimat said. "When these compounds have FDA approval, pharmacies will be utilized—but at the very bare minimum. We can do much more and many pharmacists want to do much more."

If patients mention to their pharmacist an interest in psychedelics for a mental health condition, pharmacists can counsel them on the impact their current psychiatric medications may have on the experience.

SSRIs, for example, can blunt the impact of MDMA and psilocybin and prevent patients from having a full psychedelic experience.

"That doesn't sound dangerous, but if someone is putting in hours of preparation and they're already teetering on the brink, in terms of their mental health, and they spend hundreds or thousands of dollars to have this experience, and they go to the dose day and nothing happens—then what?" Al-Olimat said.

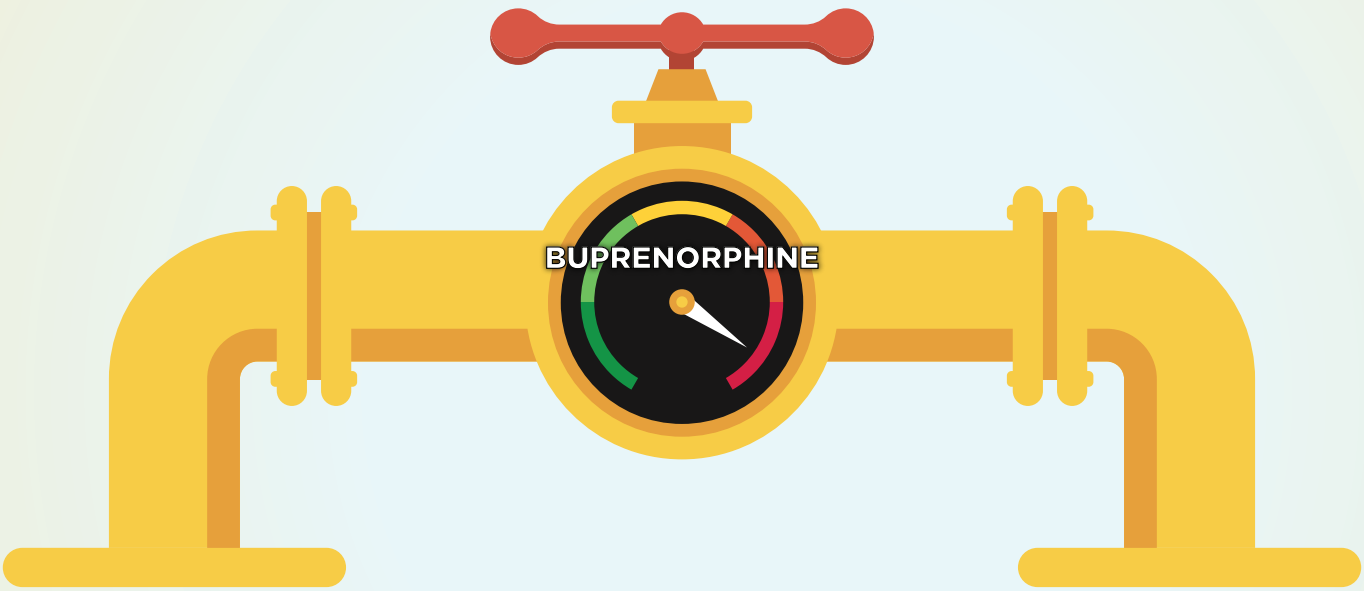
Pharmacists, he said, should encourage patients to talk to their physicians about coming off their antidepressants before trying psychedelics.

As these drugs come to market, pharmacists can be part of the patient's screening and medical intake process. They can check for and mitigate drug interactions and assist in deprescribing where needed. As some treatment protocols will call for clinical supervision on dose days, some pharmacists may train to provide that support.

## What next

Pharmacists who want to know more have options. Online courses are available, such as those offered by the Psychedelic Pharmacists Association and Spirit Pharmacist. But pharmacists might also start to carve out their role in psychedelics right in their own communities.

Search for "psychedelics" and your city on Facebook or Meetup. "You might be surprised how many local clubs you find," Al-Olimat said. "It's not a bunch of people trying to trip and hallucinate. It's just people who want a safe place to talk about psychedelics. And for you to be a pharmacist and go there—not only will you validate them, but you might also help reduce risk in your local community, which is what we should all be doing." ■




# Pharmacies face increased scrutiny over controlled medications

Loren Bonner

In Arkansas, John Kirtley, PharmD, executive director of the Arkansas Board of Pharmacy, said that several pharmacies in the state have been threatened with the loss of their ability to purchase controlled substances.

Directly, Kirtley knows of two pharmacies that were cut off by their wholesaler for controlled substance sales and were unable to get a contract with the two other main wholesalers after that action was taken.

"What we see and hear is that if one cuts you off then the other two consider that action as well and it is very difficult if not impossible for you to get a contract with one of the other two entities since they are under the same scrutiny and agreement," said Kirtley.

Wholesalers are doing all of this as part of their own DEA obligations for control and accountability in drug distribution.

"At DEA we certainly recognize that drug distributors who are selling controlled substances to pharmacies have obligations under federal law to develop systems to identify and report suspicious orders. Suspicious orders are generally orders of unusual size, pattern, or frequency," said Matthew Strait, deputy assistant administrator at DEA's Office of Diversion Control Regulatory, during a November 2023 APhA webinar.

"We don't tell distributors how much [they] can sell, we only tell them that they have to establish systems to identify and report suspicious orders. Generally speaking, those systems, which are maintained by drug distributors nationwide, set limits on what they would consider to be in a norm for purchasing patterns for a particular pharmacy."

Kirtley and others have seen issues with access to controlled substances ramp up for pharmacies in the last year or two with opioid lawsuits swirling around.

"We also hear about wholesalers flagging specific patterns of prescribing for combinations of controlled substances [opioids with either benzodiazepines or muscle relaxants] or flagging specific prescribers with action by other agencies," said Kirtley, who has done extensive work to

"We are facing both increased scrutiny in our practice across all health care providers as well as real shortages of certain controlled medications throughout our country."

address this issue with wholesalers, legislators, and pharmacies.

"Times have changed, and the supply of many controlled substances is far less than was available previously," Kirtley said. "We are facing both increased scrutiny in our practice across all health care providers as well as real shortages of certain controlled medications throughout our country."

"Take care of the person in front of you as best you can given the laws of your state and policies of your store."

**The problem with buprenorphine**

Buprenorphine seems to be the main controlled substance pharmacists won't stock—either because they don't want to exceed wholesaler limits or they can't throw off their ratio of controlled versus noncontrolled prescriptions dispensed.

"My wholesalers demand a list of physicians who write for buprenorphine alone, how many prescriptions we fill for it, quantity filled, where we purchase it from, etc.," said Tara Schneider, PharmD, an independent pharmacy owner in Lexington, KY.

She said one wholesaler told her that their numbers on buprenorphine without naloxone were too high.

"We knew that when we purchased the store in November, and have since stopped carrying buprenorphine alone," said Schneider. "We will only dispense buprenorphine/naloxone (Suboxone) and are happy to do so."

These restrictions have directly coincided with federal level efforts to increase prescriptions for buprenorphine and the numbers of individuals receiving treatment for OUD.

With the passage of the MAT Act in 2023, Congress increased health care providers' ability to prescribe buprenorphine. This legislation effectively eliminated the need for prescribers to register and fill out the X-waiver, which served to control the number of prescribers who could prescribe buprenorphine. With the X-waiver requirement removed, all clinicians, including pharmacists in certain states who hold a DEA license, are now able to prescribe buprenorphine.

"As we expect to see an increase in prescriptions written because we want more people in treatment, there's concern that these drug distributors need to be able to increase these thresholds [for] how much they will allow pharmacies to purchase," said Strait in the 2023 webinar.

During the same webinar, Valerie Prince, PharmD, former APhA president and host of the session, said that she's heard pharmacists say "I don't want to be the first one here [who] will do it, [who] will carry [buprenorphine], because then everyone will come to me, I'll get in trouble, and I won't be able to fulfill the orders anyway because distributors will be restricting me… then I might flag myself to the DEA."

Pharmacies—as well as distributors—also face legal risk carrying controlled substances.

"Through the opioid litigation at the distributor level and the pharmacy level, these companies are also reassessing their risk tolerance, which definitely has an impact on internal metrics, decision making, policies, and procedures," said Strait.

The issue is complicated and multilayered, to say the least.

**Solutions**

Strait said that controlled substance access at the pharmacy level is largely a result of business decisions being made by drug distributors.

According to Strait, one of the ways they are trying to improve access to the supply chain is by examining the underlying reasons for the thresholds that distributors are setting when they sell to pharmacies.

DEA is trying to make sure distributors understand that these quantitative thresholds can be changed and amended, according to Strait, and that DEA—the organization responsible for overseeing them—recognizes and expects an increase in prescriptions.

"Under any normal circumstance [this] may be viewed as a suspicious order, but in this particular moment and time in our nation's history, [these] are not suspicious orders. [Rather, orders for these medications] are expected to increase and we are looking forward to seeing those increases," said Strait.

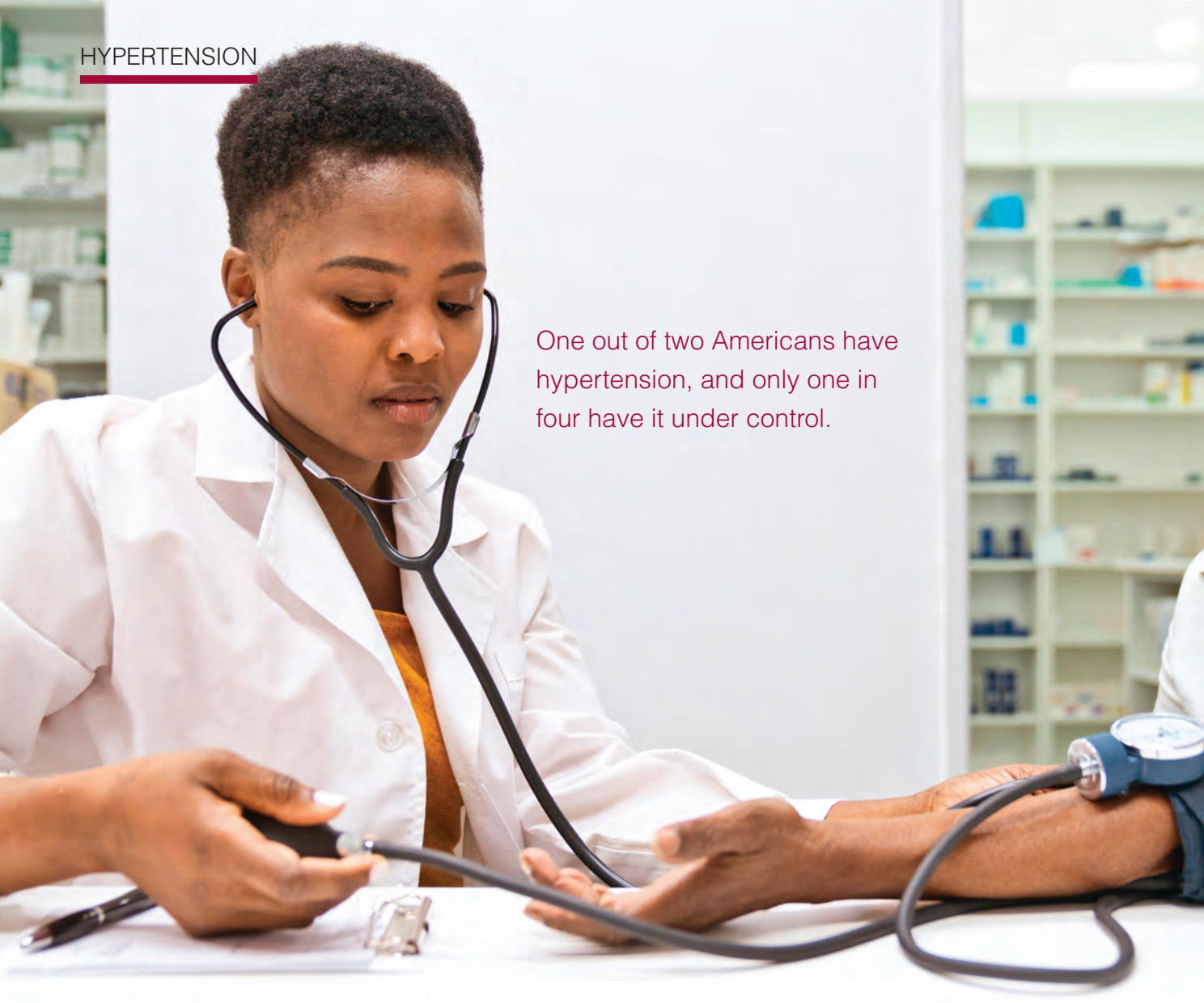
**What can pharmacists do in the meantime?**

Nicholas Carris, PharmD, who practices in Florida, said pharmacists could even try a warm introduction to another pharmacy for the patients unable to find controlled medications "to decrease the stigma of patients searching for a pharmacy to fill their medication."

"Take care of the person in front of you as best you can given the laws of your state and policies of your store," Carris said.

On the individual pharmacy level, Kirtley said communication is key. Some pharmacists in Arkansas, he noted, have done face-to-face roundtables and sharing sessions with prescribers to talk through the issues.

"Pharmacists must have positive relationships with both their patients and the prescribers sending in prescriptions so that they can have frank conversations regarding the complexities of medication supplies, especially with controlled substances," Kirtley said. ■



One out of two Americans have hypertension, and only one in four have it under control.

# CDC expanding University of Michigan pharmacist hypertension program

Loren Bonner

CDC will soon take a proven pharmacist-led hypertension program and bring it to predominantly Black populations in the southeastern United States.

The program model, which originated at University of Michigan Health in Ann Arbor, includes specially trained pharmacists who work alongside a patient's primary care physician. Patients with hypertension are seen for individualized BP control either at a primary care clinic or a community retail pharmacy—whichever is most accessible.

In 2019, CDC conducted a rigorous evaluation of the model, called the Michigan Medicine Hypertension Pharmacists' Program (HPP), and found that the program improved BP control rates for participants. Specifically, CDC found that 66% of patients who met with an HPP pharmacist had their hypertension under control within 3 months, compared with 42% of patients who did not meet with a pharmacist. At the 6-month mark, 69% had their BP under control, compared with 56% of nonparticipants.

"Given the effectiveness of the program, we wanted to explore whether the program could be implemented in a different setting and achieve similar outcomes," said a CDC spokesperson.

The agency chose the southeastern United States because it primarily serves Black populations at a higher risk of hypertension and uncontrolled BP. CDC is currently in the final stages of identifying a specific site for the program.

Hypertension affects nearly half of adults and 55% of Black adults, making it a major contributor to heart attacks and strokes, according to the American Heart Association. CDC has a goal to close this particular health disparity gap for Black adults by 5%.

After selecting a site in the southeastern region, CDC said it will provide training and support to help the program get up and running by the summer or fall of 2024.

"The goal of this effort is to understand whether the Michigan Medicine program can be implemented in a different setting with a different population and still achieve similar outcomes," the CDC spokesperson said. "If the program is effective, the HPP could be used as a model to engage pharmacists in traditional clinical settings and community pharmacies in team-based care models to broaden access to health care and improve hypertension control."

### A model is born

HPP is almost 25 years old and has expanded over the years to include select Meijer store pharmacies near University of Michigan health clinics, where pharmacists are members of the care team.

Hae Mi Choe, PharmD, clinical professor at the University of Michigan College of Pharmacy and chief population health officer for University of Michigan Health, first developed the pharmacist-centric care model in 1999. By 2009, pharmacists were embedded at clinic locations at University of Michigan Health. There, pharmacists focused on treating diabetes, hypertension, and hyperlipidemia. Choe said she started with those three disease states because the literature supports strong outcomes when pharmacists are involved in the care for these areas specifically.

"Out of those three, hypertension bubbles to the top for a couple of reasons," said Choe. Hypertension is controllable with the right combination of medication and lifestyle changes. "Blood pressure medication is effective if you stick with it, and the medications are affordable because they are mostly generics," she said.

The statistics on hypertension are alarming. One out of two Americans have hypertension, and only one in four have it under control, according to CDC.

"HPP could be used as a model to engage pharmacists in traditional clinical settings and community pharmacies in team-based care models to broaden access to health care and improve hypertension control."

### Operating within select Meijer store pharmacies

"I wanted to partner with Meijer to extend what we do in primacy care with pharmacists in the community to create more access for patients," said Choe.

To provide continuity of care from the clinic to the community, specially trained Meijer pharmacists have access to the patient's medical record. Patients are not obliged to fill their prescription at Meijer.

"It's about the service, not the fill," said Choe.

When a patient's BP is elevated during the clinic visit, a trigger is created for a clinic staff member to ask the patient if they prefer to come into the clinic or to a Meijer store pharmacy for follow-up care.

"We were able to demonstrate similar success with blood pressure being managed at the Meijer stores," Choe said.

When Choe and her colleagues did a survey of patient preferences from those who had the initial visit at Meijer, 82% picked a Meijer store for follow-up care.

### Moving forward

Pharmacists are not new to patient care services. The novel piece of it all is putting the model into practice and building connections, said Choe.

"I would strongly recommend that community pharmacies partner with physician practices and not provide services disconnected from them," Choe said. "It's important to provide continuity of care so that the right hand knows what the left hand is doing."

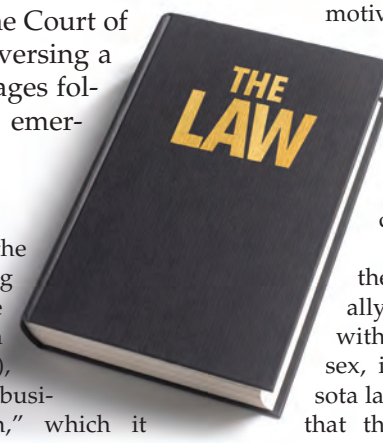
CDC plans to conduct a rigorous evaluation of the program at the new site once it's up and running.

"We will be working with the site to use their electronic health record data to understand clinical outcomes related to the program," said the CDC spokesperson. "We will also be conducting interviews with program staff to understand their approach to implementation and observing program implementation to ensure that it is happening as intended." ■

# Pharmacist liability for refusing emergency contraception prescription

David B. Brushwood, BSPharm, JD

The rights of patients and the responsibilities of health care professionals are the subject of significant litigation in the area of pregnancy termination and pregnancy prevention. The Court of Appeals of Minnesota recently released a decision reversing a jury verdict denying a patient's right to recover damages following a pharmacist's refusal to honor the patient's emergency contraception prescription.




## Background

The patient's prescription was transmitted to the defendant pharmacy. The patient called the pharmacy, and a pharmacy technician said that the drug was not in stock, but the drug would be ordered immediately so that the prescription could be processed on the following day.

The defendant pharmacist, the only pharmacist on duty, learned about the prescription and called the patient to inform her that he "refuses to dispense any emergency contraception that works by inhibiting the implementation of a fertilized egg because doing so may cause the fertilized egg to 'die,' meaning a 'new life' will cease to exist." The pharmacist also told the patient that a non-objecting pharmacist was scheduled to work with him on the following day, but that due to a predicted snowstorm, that pharmacist might not be able to travel to the pharmacy.

The patient had the prescription transferred to another pharmacy located about an hour away, and the prescription was processed for her the next day by that alternate pharmacy.

The patient sued the refusing pharmacist and the pharmacy, relying primarily on the Minnesota Human Rights Act (MHRA), which prohibits "business discrimination," which it defines in significant part to mean "to intentionally refuse to do business with a person because of a person's sex unless the alleged refusal or discrimination is because of a legitimate purpose."

A jury returned a verdict in favor of the defendants and from this verdict the patient appealed.

## Rationale

On appeal, the court noted that the defendant pharmacist had followed a policy adopted by the pharmacy that allows pharmacists to refuse emergency contraception prescriptions as long as the prescription is either honored by another of the pharmacy's pharmacists or is transferred to another pharmacy. The stated purpose of the policy is to ensure that emergency contraception prescriptions are honored.

The court then addressed the pharmacist's contention that his refusal of the prescription was not sex discrimination. The court disagreed. The MHRA provides that "sex includes, but is not limited to, pregnancy, childbirth, and disabilities related to pregnancy or childbirth." The court said the pharmacist's assertion that he was motivated by the possibility that the medication might interfere with a pregnancy, not because the patient was pregnant, was "a distinction without a difference."

The court ruled that the pharmacist intentionally refused to do business with the patient because of sex, in violation of Minnesota law. The court also ruled that the pharmacy had not refused to do business with her. The court concluded that the patient was entitled to a new trial against the pharmacist on both compensatory and punitive damages related to the business discrimination claim. The jury verdict in favor of the pharmacist was reversed. The jury's verdict in favor of the pharmacy was affirmed.

The court ruled that the pharmacist had intentionally refused to do business with the patient because of her sex, in violation of Minnesota law.

## Takeaways

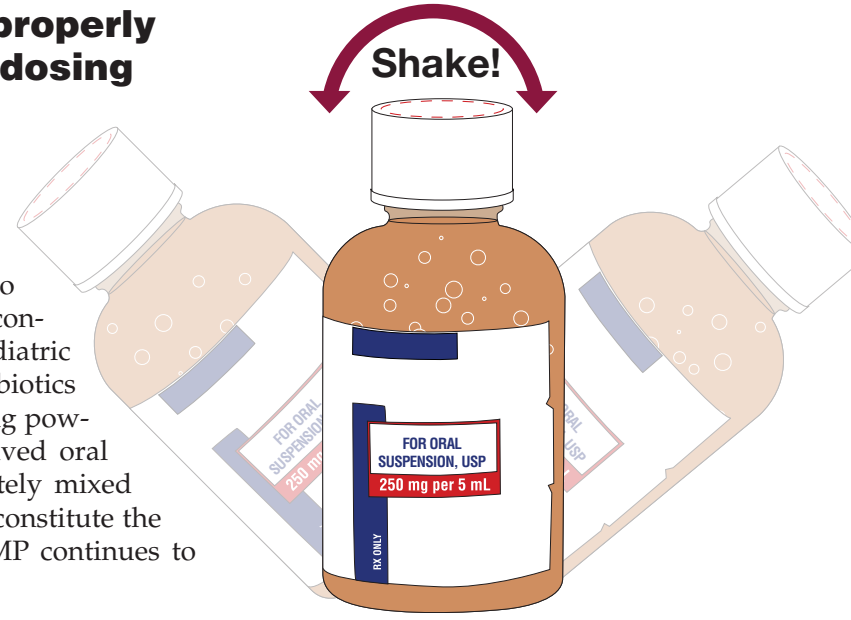
This case demonstrates that even if a pharmacist complies with a pharmacy policy allowing the conditional refusal of emergency contraception prescriptions, that refusal may nevertheless be unlawful. Pharmacists who object to such prescriptions should ensure that their objections are consistent with state laws.

The court's allowance of a new trial based on both compensatory and punitive damages exposes the defendant pharmacist to the possibility of significant economic risk. This economic risk will not extend to the pharmacy because it was dismissed from the case. An award of monetary damages may not be covered by the pharmacist's insurance.

State laws differ, and pharmacists should check with a local attorney to verify that any objections to dispensing emergency contraception are lawful. ■

# Ensure medications are properly reconstituted to prevent dosing errors and patient harm

Institute for Safe Medication Practices, Horsham, PA




The Institute for Safe Medication Practices (ISMP) has published several cases of medications being dispensed to patients before they were properly reconstituted. Most of the cases involved pediatric patients who received overdoses of antibiotics when their parents administered the drug powder to their children. Other cases involved oral suspensions that had been inappropriately mixed (e.g., not enough diluent was used to reconstitute the medication powder). Unfortunately, ISMP continues to receive reports of this type of error.

In one recent case, the pharmacy dispensed amoxicillin for oral suspension as a powder. Thankfully, the child's parent, who is a nurse, recognized that the medication needed to be reconstituted prior to administering a dose. When the parent called the pharmacy to inform them of the error, the pharmacy hung up on them.

In fact, the child's parent had to make multiple phone calls to the pharmacy before they were able to speak to someone. The pharmacy staff indicated that the pharmacy was getting ready to close and therefore the child's parent could not speak to a pharmacist. As a result of the error, the child had to wait until the next day to start their antibiotic.


In another recent case, a 10-month-old child was prescribed amoxicillin with instructions to receive 4.7 mL twice a day for 10 days. At home, the child's parents were following the instructions but ran out of medication after just 6 days. When they returned to the pharmacy to report the situation, they were informed that the pharmacy's machine that is supposed to dispense the correct amount of water for reconstitution was not calibrated correctly.

As a result, the patient's amoxicillin had been reconstituted with less water than indicated, producing a suspension with a higher drug concentration. The parents reported that the patient was experiencing dark, loose stools, fussiness, nausea, and poor appetite.

To safeguard the dispensing of oral suspensions that require reconstitution, consider the following risk-reduction strategies:

- Incorporate technology at the point of sale that will alert pharmacy staff that the prescription needs to be reconstituted. Explore options to have the alert be interactive, requiring the staff person to confirm that the medication has been reconstituted.
- Add a note or label to the prescription receipt, or use some other distinct visual cue (e.g., a brightly colored "need to mix" card) indicating that the medication needs to be reconstituted prior to dispensing.
- Place the actual product container that requires reconstitution in a separate area (e.g., not with other medications in the will-call area awaiting pickup, not bagged with other prescriptions for the patient).
- Ensure that admixture technologies are tested and calibrated on a regular basis and according to manufacturer recommendations.
- Establish a process to verify that the correct amount of liquid has been measured and used to reconstitute drugs.
- After the product is reconstituted, the product should be given to the pharmacist, along with any other prescriptions, to counsel the patient on how to measure the medication. Use the teach-back method when educating patients. Have the caregiver or patient demonstrate how they will measure and administer the dose to validate learning.
- At the point of sale, open the bottle with the patient or caregiver to check that the contents have been reconstituted.
- Ensure that an appropriate metric dosing device, which corresponds to the instructions on the label, is provided with the product.
- Include specific product descriptions on the prescription label (e.g., orange-flavored, white, opaque liquid) that will cue the consumer that they should be receiving an oral liquid product. ■

# APhA 2024 Immunization Champion Awards

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


Pharmacists have long been recognized for the vital roles that they play in delivering vaccines and providing education to patients and a wide range of other health care partners.

Millions of vaccines are administered by pharmacists and pharmacy technicians each year, and the COVID-19 pandemic 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.

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 2024 Immunization Champions, honored in March at the APhA Annual Meeting & Exposition in Orlando, have pioneered new approaches to increasing vaccination rates. Read on to learn more about the efforts and achievements of these distinguished individuals.

The 2024 APhA Immunization Champion Awards program was supported by GSK, Moderna, Novavax, Pfizer, Vaxserve/Sanofi, and CDC.

## *Individual Practitioner*

### National Winner

**Lisa B. Bade, PharmD**

**Pharmacy Clinical Care Coordinator, SpartanNash**

Lisa B. Bade has been a pharmacy clinical care coordinator with SpartanNash in Grand Rapids, MI, for the past 9 years. In this role, she coordinates and oversees the SpartanNash Immunization Program, practices as an ambulatory care pharmacist, and serves as a preceptor for the SpartanNash-Ferris State University PGY1 Community-Based Pharmacy residency program.

In addition to coordinating standing orders and immunization supply chains for the six states where SpartanNash operates, Bade immunizes patients at company clinics and events as well in her capacity as an imbedded pharmacist at Internal Medicine and Pediatrics of West Michigan (IMP-WM). Bade organized and spearheaded the pediatric COVID-19 vaccination efforts at IMP-WM, where she continues to vaccinate patients as young as 3 years old. This program is a first-of-its-kind display of private sector physician/pharmacist partnerships in Michigan.

Additionally, Bade conceived of the "Immunize at ArtPrize" initiative held at the annual ArtPrize festival in Grand Rapids. ArtPrize is a 19-day art festival in downtown Grand Rapids that attracts over a million attendees each year. Immunize at ArtPrize, in addition to providing broader access to vaccines for individuals of all ages, has helped spread public awareness about pharmacist training, capability, and roles in the immunization neighborhood. Lastly, Bade was a champion in the 2023 legislative effort that added independent immunization authority to Michigan pharmacist scope of practice with the passage of SB 219 in 2023.

Bade received her PharmD from Ferris State University in 2007 and successfully completed a PGY1 residency with Corewell Health (formerly Spectrum Health) in 2008.

Bade has dedicated most of her career to a passion: seeking, investigating, and pursuing sustainable avenues to advance the role of a pharmacist in both the primary care outpatient setting and community pharmacy setting. As a result, she has successfully developed and implemented programs that demonstrate just that. Bade has long been a member of the Michigan Pharmacists Association (MPA) and APhA. She served on the Michigan Society of Community Pharmacists Board of Directors for 9 years and now serves on the MPA Executive Board. Bade also serves with the MPA House of Delegates, has received the designation of Fellow of the MPA, has been recognized as a member of the MPA Hall of Honor, and has been awarded the MPA Pharmacist of the Year.

### Honorable Mention

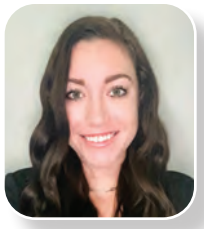
**Kaitlyn Pegump, PharmD**

**Director of Clinical Operations, Towncrest Pharmacy Corporation**

**Pharmacist-In-Charge, Towncrest Iowa City**

Kaitlyn Pegump is director of clinical operations at Towncrest Pharmacy Corporation including six community pharmacies, one long-term care closed-


door pharmacy, and one cash-based practice. Towncrest Pharmacy Corporation serves six communities in Iowa, including rural areas in which the pharmacy may be the only health care location. Pegump is responsible for the oversight of all clinical services including a robust immunization program. She not only develops all protocols, but also makes sure that each staff member is fully educated on the vaccine, understands the protocol, and is aware of the required documentation.



Towncrest Pharmacy Corporation has both pharmacists and technicians who are trained as immunizers, and Pegump oversees their training and education. Additionally, Pegump provides all employees with CDC and vaccine updates. She has spent considerable time working with each of the six community sites to increase their vaccination rates by teaching the staff to be proactive utilizing the state registry, implementing medication synchronization, and using the appointment-based model to provide clinical services including immunizations.

Pegump is the pharmacist-in-charge at the Iowa City location and also travels to each of the other community pharmacy sites to review and improve their patient care processes, evaluate their progress with clinical services (including immunizations), and provide any clinical updates.

Pegump graduated from the University of Iowa College of Pharmacy in 2021 and went on to complete a PGY1 Community-Based Residency through the University of Iowa at Greenwood Pharmacy in Waterloo, IA. After completion of her PGY1 residency, Pegump joined Towncrest Pharmacy in Iowa City, IA.

### *Corporation/Institution*

#### National Winner

**The Purdue Center for Health Equity and Innovation**

The Purdue University Center for Health Equity and Innovation (CHEqI) is a hub of interdisciplinary collaboration and community engagement highlighting the pharmacist role throughout communities in central Indiana. Through their innovative and impactful programs, CHEqI demonstrates outstanding commitment and success in addressing vaccine hesitancy and delivery among populations experiencing health disparities. At the core of CHEqI's achievements is the Community Health Access Model Program (CHAMP) led by pharmacists.

In partnership with Walgreens, food pantries, and homeless shelters, CHEqI has provided no-cost COVID-19 and influenza vaccinations to individuals facing food and/or housing insecurity, addressing vaccine hesitancy, enhancing accessibility, and mitigating health disparities in COVID-19 vaccine uptake. CHEqI administered 3,021 COVID-19 and influenza vaccines at 113 vaccination events, highlighting the positive impact of their collaborative and community-focused approach.

PURDUE UNIVERSITY
Center for Health Equity and Innovation

To build upon initial successes and continue to meet ever-changing community needs, CHAMP has expanded to include additional no-cost health services, such as naloxone distribution, tobacco cessation education, safe medication disposal kits, and BP screenings. CHEqI's work has not only improved immunization rates, but has also fostered collaboration, making pharmacists integral members of the immunization neighborhood and health care team while building trust within the central Indiana community.

#### Honorable Mention

**The Marquess Group of Pharmacies**

The Marquess Group (The Group) consists of 10 retail pharmacies in Georgia. In 2023, these 10 locations delivered nearly 35,000 immunizations of all types, including 3,000 for respiratory syncytial virus.

TMG Rx
THE MARQUESS GROUP
INDEPENDENT PHARMACY MANAGEMENT

Jonathan Marquess, cofounder and president of The Group, said "Immunizations are at the core of what our pharmacies do." He said he is proud of the work his team has done to bring immunizations to people.

This year alone, The Group conducted immunization clinics in more than 60 off-site locations. The off-site clinics help overcome the transportation issue for many low-income families. In 2023, The Group conducted clinics in factories, schools, community centers and other venues that are willing to house the 3- or 4-hour clinics. To help support these clinics, Marquess works with pharmaceutical companies, local health departments, and other organizations to provide pre-event materials describing the

**Left to right:** Mitchell Struewing, PharmD; Ashley Meredith, PharmD; Jasmine Gonzalvo, PharmD; Kaitlyn Pegump, PharmD; Lisa Bade, PharmD; Kaitlyn Priestley; Alexis Reianna Franks; Liz Moir, PharmD.

benefits of the various immunizations they will provide to those who attend a clinic.

Additionally, Marquess has worked with several pharmaceutical companies to provide immunizations to their sales people when they have meetings in the Atlanta area.

Finally, Marquess founded a company, The Institute for Wellness Education, that works with pharmaceutical companies to conduct ACPE-approved CE programs at state and national association meetings.

### *Pharmacy Team Member*

#### National Winner

**Kaitlyn Priestley, BFA, MS, CPhT-Adv**
**Pharmacy Operations Manager on Special Assignment, Immunization Services**
**Walgreens**

Kaitlyn Priestley is currently a pharmacy operations manager on special assignment for Immunization Services with Walgreens and is focused on advocating and developing resources for team members to better educate, engage, and create access to immunizations for patients across the United States.

Priestley started with Walgreens as a senior certified pharmacy technician in 2018 and was asked to champion immunizations in her pharmacy to help with connecting patients to immunization assessments, identifying gaps, and protection. During her first year in the role, Priestley identified ways to build a culture of care, influence and grow her team through coaching and resource development, and brand her pharmacy for immunization engagement.

As Priestley continued to expand her team's confidence in immunizations, she was tasked as area lead technician for immunizations, hosting immunization trainings and workshops, developing resources to be utilized across the area, supporting other stores with visits and training, and creating content for an area-wide newsletter focused on immunizations.

While in the area lead role, COVID-19 changed the immunization landscape in community pharmacy, and Priestley was asked to lead over 100 partnerships with local long-term care facilities in the Southwest Florida area to administer COVID-19 vaccines to our most vulnerable communities during the initial authorization of COVID-19 vaccines.

After returning to the store after initial COVID-19 vaccine distribution, Priestley continued her work with immunizations both in pharmacy and at an area and regional level. In late 2022, Priestley stepped out of the field and joined the Support Center for Walgreens as a pharmacy operations manager on special assignment for Immunization Services. Since her start in the role, Priestley has worked closely with teams in the field to create a feedback method to ensure a positive immunization experience for both team members and patients.

Furthermore, Priestley has helped to lead the development of trainings and resources for teams across the country and the expansion of existing immunization programs to emphasize the role of pharmacy in immunizations as well as the opportunity to protect patients fully with coadministration to address immunization gaps and address vaccine inequity driven by lack of or misinformation.

Priestley has been recognized by Walgreens in 2021 as the Area Champion of Champions for Patient Care, and by the PTCB as a subject matter expert for immunizations in 2021.

### Honorable Mention

**Alexis Reianna Franks, CPhT**

**Cavalier Pharmacy**

Alexis Reianna Franks was indispensable in aiding the pharmacy in implementing a vaccination program aimed at addressing gaps in routine vaccination coverage.

Franks assisted in nearly every step of the program. She aided in assessing patients and recording which vaccines were needed on their MedSync sheet. Franks would drop a "vaccine counseling" note in every MedSync patient chart to indicate a need to address vaccines when their medications were due. She would often have the initial conversation with the patient regarding the vaccine and then have the pharmacist follow up for more in-depth answers. Franks was instrumental in documenting and billing for the vaccines administered. She is also certified to administer vaccines when needed.

Cavalier Pharmacy's vaccination program was a success because of technicians like Franks, who really took the initiative to assist with the program in whatever way she could. She offered feedback regarding the system Cavalier Pharmacy implemented with their MedSync patients to make the program as smooth and stress-free as possible. Franks' feedback was instrumental in fine-tuning the system that was eventually rolled out to other stores that share ownership.

## *Travel Health*

### National Winner

**Liz Moir, PharmD**

**Director, Patient Care Services**

**Albertsons Companies Inc.**

Liz Moir graduated from Idaho State University with a PharmD in 2009. She began her career as a clinical staff pharmacist at Fred Meyer, a subsidiary of Kroger, where she launched their travel health program in Idaho and became the first pharmacist to obtain a yellow fever stamp. Moir joined Albertsons Companies in 2019, where she leads the development and implementation of patient-centered services that improve health and wellness.

One of her main areas of focus is travel health and immunizations, which help protect patients from preventable diseases and promote global health. She also oversees other services such as pharmacist prescribing services and point-of-care testing.

She has played a key role in expanding the scope of practice and improving access to care for patients across Albertsons locations, especially in the travel health space. Albertsons pharmacies currently offer travel health services across 29 states in 1,675 pharmacies, up from 13 states and 598 pharmacies in 2022.

This service provides travelers with essential travel health advice and pharmacy services before their trips. The program offers a travel health consultation with a pharmacist who can provide recommendations (and in many states, issue prescriptions) for travel vaccines, medications, and OTC items that may be needed during the trip based on the destination. The program covers common travel vaccines such as hepatitis A, typhoid fever, yellow fever, Japanese encephalitis, rabies, and more.

Moir believes that the program is a valuable service that can help travelers stay healthy and enjoy their adventures.

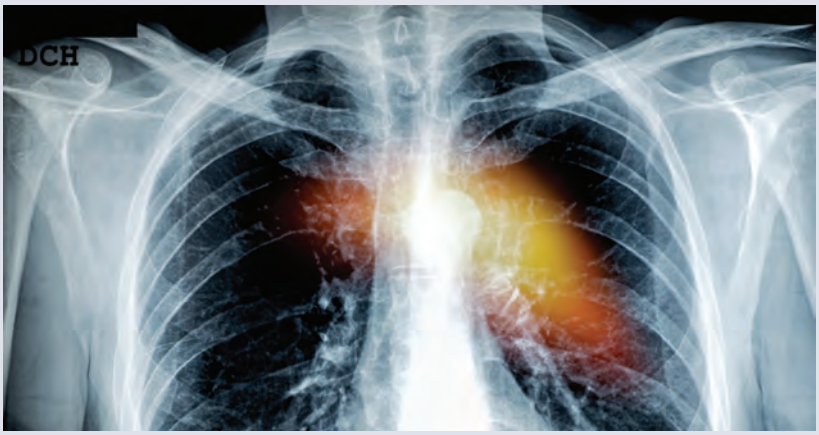
Moir is passionate about providing quality care and empowering pharmacists to practice at the top of their license. She also participates in several professional organizations and initiatives that support pharmacy innovation and collaboration and was recently recognized as one of Drug Store News' Top Women in Health, Wellness and Beauty in the Rising Stars category. ■


**Immunization delivery training available**

APhA's Pharmacy-Based Immunization Delivery Certificate Training Program is based on national educational standards for immunization training from 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 in various stages of life.

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

# Inpatient*Insights*

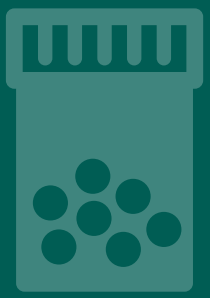



**Are anaerobic antibiotics needed for treating aspiration pneumonia?**

Although antibiotic therapy is essential for patients with aspiration pneumonia, the most appropriate type of antibiotic to use has been debated for years. A recent study, published on February 20, 2024, in *CHEST*, seeks to answer the question of whether antibiotic therapy with limited anaerobic coverage (LAC) or with extended anaerobic coverage (EAC) is most effective in terms of in-hospital mortality and risk of *Clostridioides difficile* colitis.

Researchers conducted a multicenter retrospective cohort study across 18 hospitals in Ontario, Canada, from January 1, 2015, to January 1, 2022, and included patients who were diagnosed with aspiration pneumonia and prescribed guideline-concordant first-line community-acquired pneumonia parenteral antibiotic therapy within 48 hours of admission. Patients were categorized into the LAC group if they received ceftriaxone, cefotaxime, or levofloxacin and into the EAC group if they received amoxicillin-clavulanate; moxifloxacin; or ceftriaxone, cefotaxime, or levofloxacin in combination with clindamycin or metronidazole. The primary outcome was all-cause in-hospital mortality, with a secondary outcome of incident *C. difficile* colitis occurring after hospitalization.

In the hospital, 30.3% of patients in the LAC group died, compared with 32.1% of patients in the EAC group. *C. difficile* colitis occurred in less than or equal to 0.2% of the LAC patients and approximately 1.0% of the patients in the EAC group, indicating that extended anaerobic antibiotic therapy carries an elevated risk for *C. difficile* colitis. The authors concluded that extended anaerobic antibiotic coverage is likely unnecessary in treatment of aspiration pneumonia because it is associated with no additional mortality benefit, and an increased risk of *C. difficile* colitis. ■



**Low-dose colchicine reduces CV events in patients with T2D**

The 2019 COLCOT trial demonstrated that a dose of 0.5 mg colchicine, an orally administered anti-inflammatory medication used for the treatment of gout and pericarditis, led to a significantly lower risk of ischemic CV events among patients with a recent myocardial infarction. In a study published in the March 2024 issue of *Diabetes Care*, researchers examined the trial data to determine the effect of low-dose colchicine on patients with T2D.

Among the patients enrolled in the COLCOT trial, almost 1,000 also suffered from T2D. After a median monitoring time of 22.6 months, a primary end point (CV death, resuscitated cardiac arrest, myocardial infarction, stroke, or urgent hospitalization for angina requiring coronary revascularization) occurred in 8.7% of patients in the colchicine group and in 13.1% of patients in the placebo group. Nausea was reported in 2.7% of patients in the colchicine group compared with 0.8% in the placebo group, while pneumonia occurred in 2.4% of patients in the colchicine group and 0.4% in the placebo group.

Researchers concluded that this low-dose treatment with colchicine leads to a large reduction in CV events for patients with comorbid T2D and supports results of the COLCOT trial in primary prevention of CV events. ■

### Oral iptacopan monotherapy shows promise in treating patients with PNH

Patients with paroxysmal nocturnal hemoglobinuria (PNH), a rare disease characterized by hemolysis, thrombosis, and bone marrow failure, are primarily treated with anti-C5 monoclonal antibodies. Anemia often persists, however, because of ongoing activation of extravascular hemolysis. A recent study published on March 13, 2024, in *NEJM*, investigated the efficacy and safety of iptacopan, an oral complement factor B inhibitor, in treating PNH.

Researchers conducted two phase 3 trials to assess iptacopan monotherapy over a 24-week period in patients with hemoglobin levels of less than 10 g/dL. In the first trial (APPLY-PNH), patients who were receiving anti-C5 monoclonal antibodies were randomly assigned to switch to iptacopan or to continue anti-C5 therapy. In the second trial (APPOINT-PNH), patients who had not received complement inhibitors and who had lactate dehydrogenase (LDH) levels more than 1.5 times the upper limit of the normal range received iptacopan. The two primary end points in the first trial were an increase in the hemoglobin level of at least 2 g/dL from baseline and a hemoglobin level of at least 12 g/dL, each without red-cell transfusion. The primary end point for the second trial was an increase in hemoglobin level of at least 2 g/dL from baseline without red-cell transfusion.

In the APPLY-PNH trial, iptacopan treatment was superior to anti-C5 treatment for both hemoglobin endpoints. In the APPOINT-PNH trial, treatment with iptacopan increased hemoglobin levels, reduced fatigue, reduced reticulocyte and bilirubin levels, and resulted in mean LDH levels that were less than 1.5 times the upper limit of the normal range. Mild to moderate headache was the most frequently reported adverse event in both trials. ■

### RSI intubation with rocuronium could lead to risk of awareness while paralyzed

Rapid sequence intubation (RSI) typically includes administration of induction agents to provide temporary deep sedation and prevent patient awareness of paralysis, followed by paralytic agents, including short-acting succinylcholine and longer-acting neuromuscular blocking agents such as rocuronium and vecuronium. When rocuronium is used for paralysis in the emergency department (ED), delays in sedation have been observed, but timeliness of post-RSI sedation in ICU patients has not been described. Researchers at the University of New Mexico Hospital in Albuquerque conducted a retrospective review at a single academic tertiary care center of patients intubated using rocuronium in an ICU between July 2019 and August 2020 to determine if ICU patients who receive a long-acting paralytic for intubation are likely to experience delays in sedative administration time.

The primary objective of the study, published online in *JAPhA Pharmacotherapy* on April 7, 2024, was to determine the proportion of patients in the ICU who received sedation within 15 minutes following intubation using rocuronium. Secondary objectives included determining the time to sedation (minutes) and the time to sedation between provider specialties.

Of the 192 patient intubations using rocuronium included in the study, 77 (40.1%) received sedation within 15 minutes of induction agent administration. The mean time to sedation was 25.1 minutes, in contrast to the 5-to-20-minute duration of induction agents, suggesting a potential period of time without sedation. The authors concluded that a large proportion of patients intubated in ICUs with rocuronium were exposed to risk of awareness while paralyzed. They note that future work describing appropriateness of sedation provided in both EDs and ICUs is needed to prevent awareness while paralyzed. ■

# AHA releases updates in advanced life support

Olivia C. Welter, PharmD

In January 2024, the American Heart Association (AHA) released a guideline update for CPR and emergency cardiovascular care.

Based on input from various AHA committees, the guideline document includes recommendations for clinical trial diversification, routine medication administration for cardiac arrest, temperature control, organ donation, and anti-seizure medication considerations.

### Pharmacotherapy during cardiac arrest

Within the guideline update, the authors provide insights into both vasopressor medications and nonvasopressor medications used when patients are in active cardiac arrest requiring CPR.

For vasopressors, the guideline authors recommend epinephrine administration during cardiac arrest due to the increased potential risk for coronary and cerebral perfusion during CPR. According to the guidelines, health care personnel should administer 1 mg of epinephrine every 3 to 5 minutes during cardiac arrest and, for patients with nonshockable rhythm, administering epinephrine as soon as feasible is also reasonable. For shockable rhythm, clinicians may consider initiating epinephrine after initial defibrillation attempts fail. Finally, the guidelines do not recommend high-dose epinephrine for routine use in cardiac arrest.

The authors note that no definitive evidence exists showing nonvasopressors, such as antiarrhythmic medications, magnesium, or calcium, having any positive effect on overall survival following cardiac arrest. However, administering amiodarone or lidocaine to patients with out-of-hospital cardiac arrest may improve survival during the time it takes to admit such patients to the hospital. The supporting evidence, which was reviewed by the guideline-writing group, suggested that the benefit of amiodarone or lidocaine may be time dependent as it has been most effective in cases when bystanders witnessed the cardiac arrest, allowing for emergency medical services to quickly respond.

Due to lack of demonstrated benefit, the guidelines do not recommend routine administration or use of calcium, sodium bicarbonate, or magnesium products. Steroid use during CPR for out-of-hospital cardiac arrest patients is of uncertain benefit.

### Temperature control

For cardiac arrest patients, the guidelines emphasize the importance of temperature control of the person's body, especially for those patients who are unresponsive to commands following reestablishment of their cardiac rhythm.

The benefit of amiodarone or lidocaine may be time dependent as it has been most effective in cases when bystanders witnessed the cardiac arrest, allowing for emergency medical services to quickly respond.

Historically, health care providers have used cooling devices or I.V. liquids to lower a patient's body temperature once their heart begins beating again.

In this update, the upper limit for temperature control was raised to 37.5°C with the recommendation that clinicians select a temperature between 32°C and 37.5°C at which the patient will be constantly maintained. Additionally, authors suggest that maintaining the patient at the chosen temperature for at least 24 hours after achieving the target temperature is reasonable. While a target body temperature range is provided in the guidelines, the writing group also recommends that individual hospitals develop their own protocols to follow when approaching post-arrest temperature control.

### Seizure considerations

Unfortunately, seizures are common in cardiac arrest patients who are unresponsive to commands following their cardiac rhythm being re-established. For such patients, health care providers should promptly perform an EEG and monitor continuously for the presence of seizure activity, according to the update.

Additionally, any adult cardiac arrest survivor should receive treatment for clinically apparent seizures. However, the guideline writing group emphasizes that seizure prophylaxis is not necessary and should not be routinely deployed for cardiac arrest patients.

### Other recommendations

The guidelines emphasize the importance for cardiac arrest survivors to consider becoming organ donors in the event of their death. The writing group also calls for researchers studying cardiac arrest to put in place strategies to recruit participants from diverse backgrounds for future research and to report participant demographics in published research to better quantify cardiac arrest disparities. ■

# Double duty: Treating chronic pain and CVD effectively

Ariel Clark, PharmD

Treatment plans for complex conditions can be—you guessed it—very complex. Chronic pain and CVD are two common disease states that require medication treatment, but despite the high incidence rates of both conditions, there is limited guidance for treating these conditions together.

In a study published in the February 2024 issue of *Pharmacotherapy*, Leppien and colleagues reviewed recommendations for treating chronic pain in patients who also have CVD while being mindful of potential drug interactions and safety considerations.

In 2018, CDC reported that more than 27% of Americans had two or more chronic conditions, many of which were treated by different independently practicing health care providers. Without a universal EHR system, pharmacists are often the last line of defense to protect patients from adverse events and harmful drug–drug interactions.

## Drugs that may be used with additional monitoring

Gabapentinoids and opioids can both be used in patients who have chronic pain and CVD. With these drugs, clinicians should monitor patients for fluid status changes, new onset deep vein thrombosis or other clot formation, and any increased incidence of orthostatic hypotension or syncope.

Providers should be vigilant in watching for CNS depression when using antihypertensives, opioids, muscle relaxants, and gabapentinoids—particularly in older adults who are at an increased risk for falls.

Some antidepressants and anticonvulsants are used to treat neuropathic pain or migraines. The researchers specifically mentioned the use of low-dose TCAs and SNRIs as potential options, with a preference given for SNRIs as the first line treatment.

Anticonvulsants such as carbamezapine, while effective for treating certain types of pain, should be used with caution in these patients due to their high drug interaction potential.

Clonidine and dronabinol are also commonly used in pain management for patients with both chronic pain and CVD. Clinicians can consider using clonidine as an adjunct therapy for patients with both conditions. However, researchers urge caution when considering dronabinol due to its effect on the coagulation pathway.

## What and how to monitor?

Drug adverse effects can synergistically worsen when two or more drugs cause the same adverse effect. The study authors suggested pharmacists pay special attention to these additive interactions, including possible somnolence, prolonged QTc intervals, and CNS depression, when monitoring patients with both conditions.

Baseline labs that should be collected vary depending on which drug classes are being considered. These can include baseline heart rate and BP, ECG with QTc interval, electrolytes, INR, glucose levels, A1C, and cholesterol levels. Clinicians should also continually review drug lists for medication changes that could worsen adverse effect profiles.

## Drug–drug interactions to note

Many of the drugs used to treat chronic pain and CVD are metabolized in the liver. Liver metabolism causes a number of interactions related to CYP450 enzymes.

Clinicians should be mindful of prescribing medications that share metabolic pathways. Many of the medications used to treat CVD and chronic pain are metabolized by CYP3A4, CYP2C9, CYP2D6, and CYP1A2. Induction and inhibition of these liver enzymes can significantly impact drug bioavailability and the risk of many adverse effects.

Complex conditions will continue to be a balancing act for providers and pharmacists alike when deciding which drug class to use in treatment plans.

The study authors advocated a holistic approach when deciding on a regimen. Pharmacists can review full drug lists, severity and type of pain, and adverse event risks. Working collaboratively with providers from other practice sites is imperative to ensuring patients are not put at unnecessary risk for potentially harmful drug interactions and adverse effects.

Leppien and colleagues suggested continued research into chronic pain management for patients with CVD and the development of standardized guidance supported by clinical trial data. ■

# Pharmacist-led telehealth model for psychiatric patients improves medication adherence and more

Clarissa Chan, PharmD

Pharmacist-led telehealth collaborative care has the potential to enhance treatment adherence and preventive screening for individuals with psychosis or bipolar disorder, according to findings from a January 2024 study published in the *Journal of Clinical Psychiatry.*

"People with [severe and persistent mental illness] can struggle to stay on their medications over the long term, increasing their risk for psychiatric decompensation," said Esti Iturralde, PhD, co-first study author. "[Patients] also face high long-term risk for diabetes and heart disease, so keeping up with glycemic and lipid screening is important."

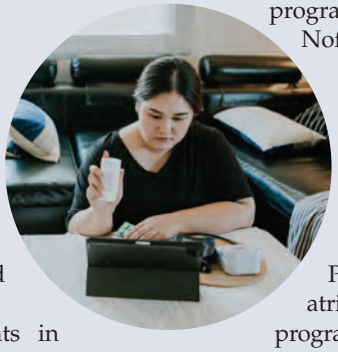
Iturralde and colleagues examined the impact of a telehealth collaborative care program at Kaiser Permanente Northern California that is managed by psychiatric pharmacists who treat adults with severe and persistent mental illness (SPMI). The retrospective cohort study compared program enrollees to similar patients receiving usual care using EHR data. Results showed that the program is associated with improved psychotropic medication adherence and glycemic screening, but unexpectedly led to a decrease in annual psychiatrist visits. Emergency department use remained unchanged.

"Offering a connection through telehealth may overcome challenges to attending appointments, providing convenient ways to stay in touch with the care team by phone or video," said Lisa Fazzolari, DO, author of the study. "These may be patients who wouldn't otherwise be seen in-person and are now getting important health screenings."

The program, called SPMI Population Care, is a team-based approach, with telehealth pharmacist visits serving as an innovative add-on to the existing team, according to Fazzolari, a psychiatrist with the Permanente Medical Group.

## Improved health care quality

The study provided encouraging evidence that integrating psychiatric pharmacist visits for patients adds value and improves the quality of their care, added Fazzolari.



"On average, patients in both groups improved in their psychotropic medication adherence during the study, but those enrolled in the collaborative care group improved more with 60% versus 50% in the usual care group meeting an optimal threshold at study's end," she said.

Compared to a control group receiving usual care without interaction from a pharmacist, the collaborative care group was also more likely to receive glycemic screening—64% versus 74%, respectively—at study end, noted Fazzolari.

The research highlights the significant role specially trained psychiatric pharmacists can play in improving health outcomes for patients with SPMI, according to Macy Shia, PharmD, program regional director, who was also part of the study.

## Considerations for pharmacists

Jill Nofziger, PharmD, who was not involved in the study, noted that gaining the support of providers early on with a program like this is key.

"Quickly establishing rapport to achieve patient buy-in with the program will help accelerate the program's success and growth," added Nofziger, who is regional ambulatory care pharmacy supervisor at Northern California Regional Clinical Pharmacy Operations.

Technology challenges may arise, too, and providing resources to triage these issues for both pharmacists and patients will help maintain workflow efficiency and reduce user frustration, Nofziger added.

"Time and resources dedicated to continued monitoring of long-term outcomes are also needed to assess the program's lasting effects," said Nofziger.

Also, consistent follow-up through a population-based model helps to build trust with patients and the mental health care team, noted Leah Arnbrecht, PharmD, a PGY2 psychiatric pharmacy residency program director and ambulatory care pharmacy supervisor within the Kaiser Permanente Healthcare system, who was not involved with the study.

## Study implications

"This study showed that pharmacists with specialized training in psychopharmacology can improve adherence to psychiatric medications and improve rates of disease prevention screening as the care continuity navigators for patients with SPMI," said Stacey Raffe, PharmD, regional clinical pharmacy director at Northern California Regional Clinical Pharmacy Operations, who was not part of the study.

"The significance for pharmacy practice includes expanding care models where pharmacists are at the center and responsible not only for the delivery of safe and effective pharmacotherapy, but coordination among the larger care delivery team," she said.

Researchers of the study are continuing to expand their evaluation of the program, which is now in 11 Kaiser Permanente Northern California service areas. They are looking at additional health outcomes, preventive care, psychiatric status, and program costs. ■

# A minute with ...

**Darren Mensch, PharmD**
**Ambulatory Care Pharmacist, Population Health**
**Jefferson Health, Philadelphia, PA**
**Member since 2011**

"Being a member of APhA has proven instrumental in allowing me to expand my network and collaborate with other pharmacists throughout the country. These collaborations have played a meaningful impact in our population health pharmacy team's ability to effectively and efficiently help our primary care offices, and most importantly, our patients."

**How has APhA helped you establish meaningful connections?**

The most meaningful connections I have developed have been within APhA–APPM's Medical Home/Accountable Care Organizations (MH/ACO) Special Interest Group (SIG). By deciding to join a SIG group's committee, it forced me to play a more active role. This culminated in my election as the MH/ACO SIG coordinator this past year. It was an honor to serve with other pharmacists across the country, and it opened numerous doors, including speaking and collaborative opportunities.

**How does APhA help you thrive in your everyday practice?**

APhA has served as a great way to bounce around ideas either through meetings with the MH/ACO Education & Resources Committee, on the ENGAGE platform, or directly with pharmacists who I met through APhA. APhA is my go-to organization when I am looking to determine if a new project is worth pursuing.

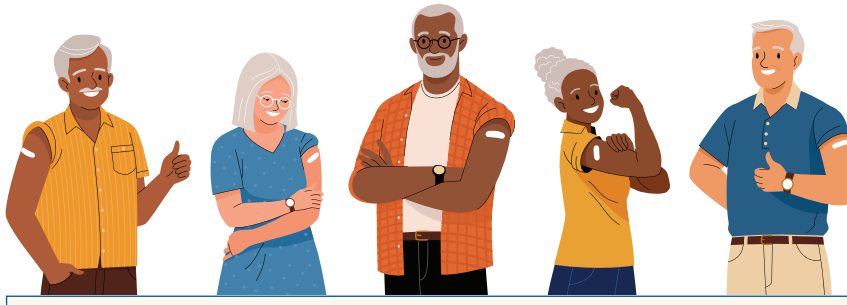
**What excites you about the profession of pharmacy?**

The innovation I have seen coming out of pharmacy is impressive. I think pharmacists are on the cusp of gaining better recognition for their efforts. Pharmacists are well-poised to disrupt America's ailing health care system.

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

I recently met with a patient who had been lost to follow-up (his last primary care provider [PCP] visit was 4–5 years ago). After he established care with a new PCP in one of my offices, his lab work came back with an A1C of 15%! He had previously been on insulin about 10 to 12 years ago following a course of steroids, but he eventually came off the medication. He saw providers off and on for a few years, but never fully established care with anyone. We started him on basal insulin, and I spoke to him for an hour after his initial provider visit. We reviewed all of his medications, including how to administer the insulin and check his blood glucose, indications of all his new medications as he was started on both a statin and BP medication, and the cost of his medications. He was clearly overwhelmed and needed a lot of clarity after his PCP visit.

During the follow-up visit after he started the insulin, he stopped me mid-sentence and said, "I just want to tell you that I had honestly given up on the health care system until you took the time to answer my questions and guide me through this. I distinctly remember how I received no guidance 10 years ago when I was started on insulin. You actually care." It's moments like these that make me excited for the pharmacy profession, and I think we will continue to foster relationships like this. ■



## Did you know?

### Free resources for your patients on the importance of lifelong vaccines

Stay informed about closing immunization gaps by keeping your patients up to date about their ongoing need for vaccines as they age with APhA's new essential resources tailored to adult immunizations and lifelong vaccination strategies. Test your knowledge of adult vaccine coadministration with our Show You Know quiz; download and explore our new informative infographic designed to show adults that they need vaccines, too; and listen to APhA's podcast series that covers coadministration guidelines, vaccine considerations across the adult lifespan, and strategies for pregnant patients.

These free-of-charge resources are supported by GSK, Merck, and Pfizer. Each item was designed to help you boost your education about keeping your patients protected. Visit apha.us/AdultImmunization to access all these resources on the APhA Adult Immunization landing page. ■

## Get involved

The APhA Transitions of Care (TOC) Special Interest Group (SIG) is an online community and professional network where pharmacists and technicians working to overcome transitional challenges can meet, share, and communicate professional interests, concerns, and prospective goals in all practice settings as they provide care to patients during transitions to and from various health care settings.

"Being part of the TOC SIG is a great experience for both new and experienced practitioners!," said Amulya, PharmD, and SIG Coordinator. "I was encouraged by a mentor to join when I was first establishing my TOC practice and I am truly thankful I did! You build a network of colleagues and friends to share ideas, work on projects, and increase awareness on the importance of TOC. I highly recommend anyone practicing or wanting to practice in the TOC setting to join!"

Visit aphanet.pharmacist.com/transitions-care to access member-only resources for all involved in providing transitions of care services. ■

## Migraine

### Are migraines impacting your patients' quality of life?

APhA's patient education guides, which are supported by Pfizer, provide comprehensive assistance to individuals grappling with migraines and offer invaluable insights into their condition, including epidemiology, symptomology, and pathophysiology.

Delving deeper, they explore the contributing factors and triggers such as stress and insomnia alongside effective headache monitoring and trigger management techniques. Moreover, they meticulously outline pharmacotherapy options, emphasizing adherence and methods for improvement, while also presenting nonpharmacologic alternatives like relaxation techniques, biofeedback, and cognitive behavioral interventions.

Additionally, they offer guidance on communication strategies, equipping patients with resources to effectively engage with caregivers, family, friends, health care professionals, and coworkers about their migraine journey, fostering a sense of support and understanding. Visit www.pharmacist.com/Education/Management-and-Support-for-Migraine-Patients for a downloadable PDF of each flyer. ■

# A patient's journey with migraine

**Richard Wenzel, PharmD, CPPS,** consultant pharmacist, Chicago Headache Center and Research Institute, Chicago, IL; and pharmacist, Pain Navigation & Medication Optimization, Indiana University Health, Indianapolis, IN

Migraine headache is a major public health concern, being the sixth most prevalent disease worldwide and affecting more than a billion people of virtually every ethnicity, age, socioeconomic status, family relationship, geographic location, or overall health.[1,2] Despite migraine's commonness, this illness remains under-recognized and undertreated, resulting in considerable debilitation, reduced quality of life, pain, and economic burdens.[3,4] Opportunities to reduce these adverse consequences include increasing migraine diagnosis, improving patient education, enhancing access to and use of migraine-specific medications, optimizing nondrug therapies, and routine evaluations of care.

WHO specifies lack of clinician education as a principal barrier toward advancing migraine care.[5] A survey of U.S Colleges of Pharmacy identified opportunities to improve didactic migraine education.[6] Other research illustrates similar needs for clinicians such as physicians and nurses; the American Headache Society (AHS) has specifically called for enhancing primary care providers' training and abilities, and other research advocates expanding pharmacists', psychologists', and other allied health professionals' roles in treating individuals with migraine.[7,8]

## Epidemiology

Per the Global Burden of Disease study, migraine's general population prevalence is 14%; thus, migraine is more prevalent than other chronic illnesses such as diabetes (12%) or asthma (8%).[9–11] Migraine's peak prevalence occurs approximately between the ages of 25 and 50 years old, which are years of peak adult productivity—career advancement, child-rearing, major financial obligations (e.g., home mortgage), and other adult ambitions.[9,12–15] Unfortunately, migraine's hallmark feature is recurrent attacks causing debilitation: the inability to perform usual work, home, or social activities or reducing performance by at least 50%. As a result, among individuals under the age of 50 years old, migraine is the world's second leading cause of debilitation, resulting in billions of dollars of lost productivity, among other negative consequences.[14] Migraine's impact disproportionately affects women, with a 17% female versus 6% male prevalence.[12]

In clinical practice, patients and clinicians often view migraine strictly in terms of "attacks," a conceptualization that assumes headache-free times are

### Patient scenario

JW, a young adult woman previously unknown to you, presents to your community pharmacy wearing sunglasses on a cloudy day. She expresses that "my head is killing me; I'll probably miss work again this afternoon" and asks "Do you have something that can help?"

Upon inquiry, JW reports that she has been self-treating her headache attacks with ibuprofen for "about a year," remarking exasperatedly that "ibuprofen doesn't seem to help anymore, but I take these pills nearly every day because I don't know what else to do."

**Learning objectives**

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

- Describe migraine headache diagnostic criteria, epidemiology, and medication use patterns.
- Compare and contrast evidence-based pharmacological and nonpharmacological acute and preventive migraine treatment options.
- Describe methods to assess patients presenting to a community pharmacy with a complaint of headache to determine appropriate over-the-counter therapies versus a referral to a physician.
- Identify appropriate use of validated questionnaires to diagnose migraine, assess disease burdens, and evaluate medications' effectiveness.
- Describe validated methods to identify patient-specific factors that may contribute to a migraine attack's initiation.
- Given a patient scenario, formulate a migraine treatment plan.

**Preassessment questions**

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

1. **To assess how headaches currently impact JW's life, you should recommend:**
   a. That she get a head X-ray at a local emergency department.
   b. That JW complete a validated assessment tool such as MIDAS or HIT-6.
   c. That you should speak to her boss for input.
   d. That she rate her current pain on a 10-point scale.

2. **You should recommend that JW seek a physician's evaluation because:**
   a. She is experiencing daily headaches.
   b. She is experiencing debilitation (unable to work).
   c. Her ibuprofen consumption constitutes overuse, which can contribute (and for JW likely is contributing) to worsening headaches.
   d. All of the above.

3. **To help identify factors that may be contributing to her headache attacks, JW should:**
   a. Maintain a headache diary.
   b. Skip all meals for 24 hours.
   c. Eliminate chocolate, alcohol, caffeine, and monosodium glutamate from her diet.
   d. None of the above.

correspondingly free of consequences. Yet migraine can exert harms during non-attack times, a phenomenon known as interictal burden.[16,17] This burden can include fear that an attack may strike at an inopportune moment at work, school, or social settings; avoidance or changing of daily life activities; or financial consequences.[18] Individuals with migraine may be stigmatized by society at large; for example, family, friends, or work colleagues incorrectly labeling someone with migraine as being less able or not able to cope with life's daily hassles. This stigma can contribute to poorer migraine health outcomes, among other negative results.[19–21] Importantly, migraine's impact extends beyond the person with this illness; for example, half of the spouses of people with migraine report reduced enjoyment of their relationship.[22]

## Pharmacists and migraine

In recent decades, a complaint of headache consistently ranked among the leading reasons people sought a pharmacist's consultation; according to 2023 data, pharmacists made approximately 83,000 "migraine headache product" as well as 62,000 "headache product" recommendations daily.[23–27] Some—and perhaps most—of the "headache product" recommendations may be for individuals with migraine who are undiagnosed or misdiagnosed. This commonality of interactions with people with migraine strategically positions pharmacists in community pharmacies to:

- Identify and refer undiagnosed or misdiagnosed individuals.
- Provide disease and medication education.
- Identify and educate patients at risk of acute medication overuse.
- Help patients recognize modifiable lifestyle behaviors or other factors that may worsen attacks' frequency or severity.
- Help guide selection of effective pharmacological and nonpharmacological therapies, including recently approved treatments.
- Assess treatments' benefits, or lack thereof, and orchestrate changes when necessary.

**Patient scenario *continued***

Regarding her attacks' symptoms, JW experiences "bad head pain. The sun bothers me, my earlobes feel flush, and I skipped breakfast this morning because my stomach cannot handle food right now. And the inside of my head just pounds and pounds like a drum. I know this will not go away until tomorrow or the next day."

## Diagnosis

In the United States, approximately 38 million adults experience headache attacks that fulfill International Headache Society (IHS) migraine diagnostic criteria.[28,29] Six out of ten people with migraine are clinician-diagnosed; thus, 4 out of 10—roughly 15 million people—remain undiagnosed.[3] Incorrect self-diagnosis (e.g., as tension headache or as sinusitis), self-treatment, and lack of clinician consultation are common reasons for

**International Headache Society migraine without aura diagnostic criteria**

A. At least five attacks fulfilling criteria B–D.
B. Headache attacks lasting 4 to 72 hours (untreated or unsuccessfully treated).
C. Headache has at least two of the following four characteristics:
   1. Unilateral location.
   2. Pulsating quality.
   3. Moderate or severe pain intensity.
   4. Aggravation by or causing avoidance of routine physical activity.
D. During headache at least one of the following:
   1. Nausea and/or vomiting.
   2. Photophobia and phonophobia.
E. Not better accounted for by another diagnosis.

Source: Reference 28.

underdiagnosis and misdiagnosis.[30]

The IHS primary headache diagnostic criteria, which describe more than 100 headache disorders, are themselves a diagnostic impediment.[28] These criteria were originally developed for clinical trials, not for day-to-day practice, and can be cumbersome to use even for clinicians familiar with their application.[28,31] Many IHS categories are not mutually exclusive; for example, during a single headache attack, a patient's symptomatology can evolve so that at one moment their headache fulfills tension headache criteria, yet at a later moment the same attack fulfills migraine criteria. This lack of distinction can yield diagnostic uncertainty and impact treatment decisions.[32] An accurate IHS diagnosis also depends on patients' abilities to recall specific symptoms that may have occurred weeks or months ago.

Ideally, migraine would be diagnosed via an objective biological marker of disease. Similarly, assessment of migraine's severity as well as treatments' effectiveness would utilize an objective marker. Unfortunately, such a marker eludes current scientific knowledge; lack of a biological marker of disease remains a key barrier toward improving migraine diagnosis and treatment, although ongoing research may produce such a test in the future.[33] Until then, pharmacists should adopt a general rule that all patient-reported, recurrent, and debilitating headache attacks are migraine until information demonstrates otherwise.

## Medication use patterns

Medication use among individuals with migraines is common; 97% currently use either a prescription, OTC acute medication, or both.[3] Paradoxically, medication underuse also persists; 40% meet eligibility criteria for migraine preventive drugs, yet only 17% are prescribed these medications.[3] Among patients prescribed a preventive drug, 70% either switch or discontinue that drug within 6 months due to concerns about efficacy or tolerability/safety; these concerns suggest inadequate patient education, a shortcoming that could be resolved via pharmacist medication counseling.[34]

Even when medications are prescribed, the desired outcome may not be attained: surveys report that 50% experience inadequate pain freedom at 2 hours after taking the medication dose, and 38% must cope with headache recurrence within 24 hours after taking the medication.[35,36] Such data suggest issues with medication selection or nonoptimal drug administration; for example, delaying consumption of an acute medication until an attack's intensity is severe.

Medication-overuse headache affects up to 7% of the general population—over 20 million people in the U.S.—and has been ranked among the top 20 disorders worldwide, causing years of life lost due to debilitation.[37] Commonly overused drugs include OTC analgesics and opioids.[38] Whether acute drug overuse is a cause of, or a consequence of, increased migraine frequency and severity remains a matter of debate.[39] Regardless, continual escalation of acute migraine drugs use has been identified as a modifiable risk factor for migraine frequency and severity progression.[40]

Unfortunately, nearly half of people with migraine have been prescribed an opioid in their lifetime, and 19% currently use these medications despite no opioids being approved by FDA for this purpose, robust evidence of their adverse consequences compared to other treatments, and guidelines specifically discouraging their use.[3,41] Conversely, seven triptan medications (sumatriptan, zolmitriptan, rizatriptan, naratriptan, eletriptan, almotriptan, and frovatriptan) are approved by FDA and guideline-endorsed, yet only 35% of people with migraine have been prescribed triptan medications in their lifetime, and only 23% currently use triptans.[3]

These data suggest suboptimal therapy; pharmacists should prioritize the identification of people using opioids or other medications lacking evidence of efficacy for migraine and encourage these individuals to seek a headache specialist's evaluation. Patients can find a physician specifically trained to treat migraine (or other clinician trained to diagnose and treat migraines, such as a physician assistant or nurse practitioner) by searching patient advocacy organizations' resources. For example, the National Headache Foundation offers a "Find Certified Providers" option at www.headaches.org/resources/healthcare-provider-finder/, while the American Migraine Foundation has a similar tool at www.americanmigrainefoundation.org/find-a-doctor/.

**Patient scenario *continued***

JW states that a year ago, she only took ibuprofen "maybe a few times per month." However, recently she realized that she had consumed an entire 100-tablet bottle in just 1 month, mainly due having some level of head pain almost every day. However, she states that "attacks" happen perhaps once or twice per week. She asks for a recommendation for a drug to replace her ibuprofen.

## Newly approved medications

In recent decades, research illuminated the role of calcitonin gene-related peptide (CGRP) as an important substrate in the pathophysiology cascade that results in migraine attacks' occurrences.[42,43] During attacks, CGRP levels are elevated in plasma, saliva, tears,

and cerebral spinal fluid.[42,43] Moreover, infusing CGRP into a person can induce a migraine-like headache. These insights led to developing medications that target either CGRP's ligand or CGRP's receptor, disrupting the pathophysiology cascade and thereby minimizing CGRP elevations and reducing the occurrence of attacks or bringing an ongoing attack to resolution.[44]

Today, FDA labels approved migraine drugs acting on the CGRP cascade as a "CGRP antagonist."[45–52] Medical literature and other information sources may further divide these drugs into CGRP monoclonal antibodies (CGRP mAbs)—erenumab, fremenezumab, galcanezumab, eptimezumab—and gepants—atogepant, rimegepant, ubrogepant, and zavegepant.[53,54]

## CGRP mAbs

Table 1 provides CGRP mAbs' pharmacologic highlights.[45–48]

These medications represent an important milestone, as they are the first preventives specifically conceptualized and developed to treat migraine.[55,56] All previous migraine preventive drugs were originally developed for other illnesses. Each CGRP mAb is indicated for migraine prevention in adults.[45–48] Summarizing their clinical trials' results, versus a placebo these drugs significantly reduced the number of monthly migraine days by approximately 1 to 3 days, while several secondary measures were also significantly reduced, such as a 50% reduction in monthly migraine headache days and acute medication usage.[54,57–59]

CGRP mAbs offer several distinctions compared to long-used migraine preventive drugs. Their reduced frequency of administration–that is, monthly or quarterly–may be preferable to patients versus the daily administration of existing migraine preventives. CGRP mAbs are generally well-tolerated, and their tolerability profile stands in contrast to drugs historically prescribed for prevention; the adverse effects (AE) of antiepileptics, tricyclic antidepressants, beta blockers, and other agents are well described, common, and often caused discontinuation or tolerability issues that increased migraine treatment complexity.[58] CGRP mAbs' improved AE profile can be an important advantage compared to existing therapies.

Of note is that after launch, FDA added information to erenumab's Warnings and Precautions statements regarding constipation as well as hypertension; such statements are not contained in other CGRP mAbs' labeling.[45]

## Gepants

Table 2 highlights gepants' characteristics.[49–54]

Rimegepant is the only medication approved by FDA for acute as well as preventive migraine therapy in adults. For acute use, this drug's dose is 75 mg once as needed. For prevention, the recommended dose is 75 mg every other day. Pharmacists should ensure that this atypical dosing frequency is communicated to patients and should discuss how to best manage missed doses. For either indication, the maximum rimegepant recommended 24-hour dose is 75 mg; when used for prevention, on nonscheduled dose days an as-needed acute 75 mg dose can be used.

Rimegepant's formulation is an orally disintegrating 75 mg tablet that is administered via an oral or sublingual route. The sublingual route may be advantageous for patients experiencing nausea with attacks.

Zavegepant is administered via a single-use intranasal device. Pharmacists should review specific device usage instructions with patients.

Similar to CGRP mAbs, gepants tend to be well-tolerated, an important distinction versus drugs historically used for migraine prevention.[59] Ubrogepant, rimegepant, and zavegepant lack the cardiac AEs that can be concerns with other FDA-approved acute drugs such as triptans or dihydroergotamine.

## Medication selection

Choosing the "best" CGPR mAb or gepant on the basis of available efficacy or tolerability data can be a difficult exercise.[61] Thus, selection typically involves sorting through frequency of administration, route of administration, costs, or other patient-specific preferences.

Inadequate response to one CGRP

**Table 1.** Calcitonin gene-related peptide monoclonal antibodies

| Medication | Route and administration | Dose | Frequency | Comments |
|---|---|---|---|---|
| Erenumab-aooe | Subcutaneous autoinjector | Initial dose 70 mg, although some may benefit from 140 mg initially, then 70 mg thereafter | Monthly | • 140-mg and 70-mg autoinjectors<br>• Labeling has unique constipation and hypertension Warnings and Precautions |
| Fremanezumab-vfrm | Subcutaneous autoinjector | Either 225 mg or 675 mg | Monthly (225 mg) or quarterly (675 g) | • 675 mg = three 225-mg injections<br>• Also available as a 225-mg prefilled syringe |
| Galcanezumab-gnlm | Subcutaneous autoinjector | Loading dose of 240 mg, then 120 mg thereafter | Monthly | • 240 mg = two 120-mg autoinjectors<br>• Also available as a 120-mg prefilled syringe |
| Eptimezumab-jjmr | Intravenous infusion | 100 mg, although some patients may benefit from 300 mg | Quarterly | Administered by trained personnel |

**Table 2.** Gepants

| Medication | Dose | Comments |
|---|---|---|
| Ubrogepant | 50 mg or 100 mg orally, repeated in 2 hours if needed; maximum 200 mg per 24 hours | • 50 mg for hepatic or renal impairment<br>• Contraindicated with strong CYP3A4 inhibitors |
| Atogepant | 10 mg, 30 mg, or 60 mg orally once daily | 10 mg for renal impairment |
| Rimegepant | Acute: 75 mg orally or sublingually once as needed<br>Prevention: 75 mg orally every other day | • Orally disintegrating tablet<br>• Only medication for both acute migraine and prevention<br>• Drug interactions with CYP3A4 inhibitors/inducers and P-gp inhibitors |
| Zavegepant | 10 mg (one spray) into one nostril as needed; maximum 1 spray per day | Teach patients nasal device usage |

mAb or gepant is not predictive of the response to a different medication in these classes.[62–66] These drugs can be concurrently prescribed with other migraine acute and preventive medications.

Since the CGRP mAb and gepant approvals, a debate has existed among headache specialists as to whether patients must fail a trial(s) of older, less costly, and often poorly tolerated but nevertheless guideline-endorsed migraine preventive medications prior to being prescribed a newly approved drug.[67,68] Additionally, in clinical practice most insurers require failure of older medications before reimbursing the new, more costly medications.

However, in March 2024, AHS updated their position statement regarding CGRP mAbs and gepants: "The CGRP-targeting therapies should be considered as a first-line approach for migraine prevention along with previous first-line treatments without a requirement for prior failure of other classes of migraine preventive treatment."[69] Per this updated statement, the evidence supporting CGRP mAbs' and gepants' first-line recommendation is "substantial in its volume, scope, and quality."[69]

Besides their ability to reduce the frequency of attacks, these drugs have improved adherence and efficacy in patients with prior treatment failures and they can be beneficial in instances of acute medication overuse. Moreover, migraine "cost" considerations should not be limited to merely drug acquisition prices; rather, the totality of direct and indirect disease costs must be tallied, including less effective or poorly tolerated treatments' increased health care resource utilization (e.g., emergency department visits); missed family, social, and work activities; patients' suffering from pain and other symptoms that could have been avoided; and the negative impacts on family members.

The updated AHS statement notes that older medications may be the most efficient therapies to address migraine concurrently with a comorbidity; for example, hypertension or depression.[69] In these instances, a beta blocker or serotonergic drug may be the best option, respectively.

## Patient safety

Administration errors have occurred due to variations among CGRP mAbs' and some gepants' doses, routes, or frequencies of administration. For example, in clinical practice there are stories of patients inadvertently activating autoinjectors' release buttons too soon, thereby squirting (and wasting) the medication onto the floor.[70] FDA's Adverse Events Reporting System has dozens of reports of "product dose omission issue," "underdose," "inappropriate schedule of product administration," and other similar issues.[70] For instance, galcanezumab's loading dose is 240 mg, but this drug is only available for migraine in a 120-mg autoinjector or prefilled syringe; misunderstandings have led to patients injecting just one autoinjector, rather than the intended two autoinjectors.

Similar misunderstandings about the correct number of autoinjectors needed for a prescribed dose have occurred with erenumab and fremanezumab. These examples highlight the importance of pharmacists providing effective patient education about medication and device usages.

## Other FDA approvals

Lasmiditan was originally studied for migraine more than a dozen years ago but did not attain FDA approval until 2020.[71–73] Lasmiditan is the only serotonin 1F receptor agonist drug for migraine and is indicated for the acute treatment of attacks in adults. Lasmiditan is available in 50-mg and 100-mg tablets, and the recommended dose is 50 mg, 100 mg, or 200 mg once as needed; all three doses are superior versus placebo at attaining 2-hour pain freedom as well as relief from a patient's most bothersome symptom.[73] Lasmiditan should not be taken more than once per 24 hours, as a second dose during the same migraine attack was not demonstrated to be beneficial.[73] The safety of treating more than four attacks in a 30-day period is not known. Tolerability is similar across all three doses. Lasmiditan has few cardiac AE concerns, in contrast to other acute drugs such as triptans or dihydroergotamine.

**Patient scenario *continued***

JW asks "What causes these headaches? My coworker says that I have migraine, but I don't believe her. I think these are just tension headaches because they stress me out."

Unique among acute migraine medications, lasmiditan is a Schedule V drug with a Warnings & Precautions labeling statement advising patients "not to engage in potentially hazardous activities requiring complete mental alertness, such as driving a motor vehicle… for at least 8 hours [post-dose]."[73] For most adults, engaging in many of life's daily activities depends on driving a vehicle. Moreover, returning patients to normal function is a key goal of acute

migraine therapy. Thus, rationalizing lasmiditan as a treatment-of-choice option is difficult. Instead, this drug's optimal role may be for when other acute agents are ineffective, not tolerated, or some other patient-specific factor necessitates lasmiditan's use.

### Patient-reported outcome measures

Patient-reported outcome measures (PROMs) from easy-to-use questionnaires have been validated for various purposes including to facilitate migraine's diagnosis, quantify and qualify disease burdens, and assess treatments' effectiveness.[74,75] These tools are endorsed by IHS; utilized by FDA during migraine drug approval processes; and recommended for systematic reviews, observational studies, and other research purposes.

Expanding the distribution and use of PROMs within community pharmacies and other clinical environments should be a priority for pharmacists. Pre-printed copies could be made available for patients or displays with electronic access links (such as a QR code) can be posted within pharmacies, enabling patients to complete the tool on their electronic devices. Once completed, results can help patients gain greater understandings about their illness' impacts, inform treatment selections, and identify patients who are appropriate for referral for a physician's evaluation. Several PROMs are available for public use at www.headaches.org/resourses/headache-tests/.

Several tools can help quantify or qualify the negative impact migraine imposes on a person's ability to engage in life's daily activities as well as assess therapies' benefits. Such tools can:

1. Provide a snapshot of migraine's current impact, which can also serve as a baseline.
2. Be readministered at future dates to inform patients and clinicians of treatments' effectiveness and prompt therapy changes.

### ID Migraine

The ID Migraine tool is a validated, reliable, easy-to-use migraine screening questionnaire.[76] Answering the three "yes" or "no" questions can typically be completed in a minute or less. A "yes" to at least two of the questions is highly predictive of a person meeting IHS migraine diagnostic criteria; pharmacists should counsel any person with at least two "yes" answers to consider a physician's evaluation.

### MIDAS

The five-question Migraine Disability Assessment Questionnaire (MIDAS) can usually be completed in minutes and assesses the number of days this illness negatively impacted work, school, household, and social activities during the preceding 90 days.[77] After tallying a patient's responses, the resulting number will correspond to:

- Score of 5 or less, Grade I, little or no disability.
- Score of 6 to 10, Grade II, mild disability.
- Score of 11 to 20, Grade III, moderate disability.
- Score of 21+, Grade IV, severe disability.

Patients with MIDAS Grade I are appropriate for OTC medications exclusively.

Individuals with MIDAS Grade II may or may not be appropriate for exclusive OTC drug use, depending on other patient-specific issues. For example, is nausea and vomiting occurring? If so, a prescription antiemetic may be needed.

People with Grade III or Grade IV are poor candidates for exclusively treating with OTC medications; these individuals should be referred for an evaluation and, likely, prescription therapies.

The MIDAS tool was studied in a community pharmacy setting.[78] Results showed that the majority of people seeking a pharmacist's OTC medication recommendation were MIDAS Grade III or IV and thus were experiencing migraine debilitation unlikely to respond to OTC therapies.[78] Nevertheless, they were seeking a pharmacist's recommendation for an OTC product; these individuals were appropriate for a physician's referral and prescription therapies.[78]

### HIT-6

The validated, six-question Headache Impact Test (HIT-6) assesses migraine-related debilitation in the preceding month.[79] This tool can typically be completed in a few minutes, with patients' responses tallied for a numerical score. Although scores do not correspond to a specific category, the higher the score, the greater likelihood a person needs a physician's evaluation and prescription therapies.

### Migraine-ACT

Specific to acute medications, the validated, four-question Migraine-ACT tool's "yes" or "no" answers help determine these drugs' effectiveness and illuminate the need for changes.[80,81] Patients answering "no" to at least one question require medication evaluation and, most likely, modifications.


## Accreditation information

Provider: APhA
Target audience: Pharmacists
Release date: May 1, 2024
Expiration date: May 1, 2027
Learning level: 2
ACPE Universal Activity Number: 0202-0000-24-207-H01-P
CPE credit: 1 hour (0.1 CEU)
Fee: There is no fee associated with this activity for APhA members. There is a $25 fee for nonmembers.

APhA is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education (CPE). The ACPE Universal Activity Number assigned to this activity by the accredited provider is 0202-0000-24-207-H01-P.
Advisory board: Katie Meyer, PharmD, Sr. Director, Content Creation, APhA, Washington, DC.

Disclosures: Richard Wenzel, PharmD; Katie Meyer, PharmD; and APhA's editorial staff declare no conflicts of interest or financial interests in any product or service mentioned in this activity, including grants, employment, gifts, stock holdings, and honoraria. For complete staff disclosures, please see www.pharmacist.com/apha-disclosures.
Development: This home-study CPE activity was developed by APhA.

The Migraine-ACT can typically be administered quickly and easily and be periodically readministered to confirm drugs' effectiveness, particularly after acute drug changes.

**Patient scenario *continued***

In your pharmacy, JW completes a MIDAS questionnaire on her cellphone, which shows Grade III debilitation. She asks you what this means.

Pharmacists should seek to document the result of PROMs in a patient's chart for future reference. These tools' results can also help support an individual to overcome hesitancy about certain medications. For example, a person reluctant to use an injectable drug may become more agreeable to a trial of that medication upon learning that a tool indicates their attacks are "severe" and thus appropriate for injectable therapy.

## Pharmacist OTC recommendations

When an individual seeks a community pharmacist's recommendation for an OTC headache medication, the key determination is whether the person is suitable for exclusively using OTC products versus needing a referral to obtain prescription and other therapies.[23,24,82] A proposed algorithm can help pharmacists promptly assess a person's appropriateness for OTC therapies exclusively:

### Question 1: Are the majority or minority of your headache attacks debilitating?

Patients answering that the majority of their attacks result in debilitation—the need for bed rest; inability to perform usual home, work, and social activities; or such ability reduced by at least 50%—are poor candidates for OTC options exclusively; referral to a physician should be considered. Clinical drug trials of OTC migraine medications have consistently excluded people experiencing debilitation with 50% or more of their attacks, and guidelines specifically endorse OTC drugs for "mild" or "non-incapacitating" attacks.[23,24,67,82] Thus, available data do not demonstrate OTC therapies' benefits for people with higher debilitation levels.

### Question 2: How many days per month are you completely headache-free?

Patients answering that they are headache-free 15 or fewer days per month (in other words, they experience headaches 15 or more days per month) meet IHS criteria for chronic headache.[28] These individuals are poor candidates for OTC therapies exclusively, and a physician's referral should be considered. Moreover, these individuals are at risk of overusing acute medications, including OTC products, which is a known risk factor for worsening headaches' frequency, severity, and duration.[37,38]

If question 1 or 2 results in a referral, then questions 3 and 4 are unnecessary. If a referral is not prompted, then questions 3 and 4 should be asked.

### Question 3: What symptoms accompany your headache attacks?

Patients reporting any of the following may benefit from an OTC migraine product recommendation:

- Sensitivity to light or sound.
- Pain (whether mild, moderate, or severe).
- Unilateral or throbbing pain.
- Aggravation of pain/symptoms with routine activities.

### Question 4: What OTC products have you already used or are presently using to treat your attacks?

This question elicits what medications might currently be beneficial as well as any prior medication failures, which is information that can affect a pharmacist's recommendation(s) of OTC medications.

OTC migraine medications approved by FDA, endorsed by AHS, or both, include acetaminophen, ibuprofen, naproxen, and aspirin as well as combinations of these drugs with caffeine.[23,24,82]

People who have never utilized an OTC product for migraine can select among any of them; available data do not demonstrate the superiority of one OTC product versus another. People who have unsuccessfully tried one product can opt for a different OTC agent. Pharmacists and patients should ensure that the failed OTC products were distinct; several OTC agents have different brand names yet contain identical or nearly identical active ingredients, which can result in mistakenly believing that two supposedly "different" products have been used.

Individuals who have tried and failed two or more OTC acute medications should consider a physician's referral.

In clinical practice, one definition of "failure" of an acute OTC medication is the drug not providing adequate relief—as defined by the patient—in the majority of attacks. For example, if a drug was consumed during the four most recent attacks, but the drug only relieved one of those attacks, then this should be considered failure. In OTC failure instances, options include increasing that drug's dose or redosing the medication (e.g., 2 hours after the first dose) within permissible daily dose limits or switching to a different medication(s).

Pharmacists and patients should be aware that previously effective OTC drugs may lose effectiveness over time.

**Patient scenario *continued***

JW's coworker told her to stop eating chocolate and to switch laundry detergents, and JW wonders if this was good advice.

As endorsed by migraine treatment guidelines, patients should be counseled to limit their total acute medication intake to 2 days per week.[23,24] Avoid confusing "days" with "doses"; many acute medications can be dosed multiple times during a 24-hour period, and these multiple doses only constitute 1 day. There are a few exceptions to this limit; for example, consumption of OTC NSAIDs for 5 consecutive days is a common treatment for menstrual migraine.[83] Nevertheless, any individual consuming acute drugs more than 2 days per week for weeks or months without end is at risk of worsening

headaches; a referral should be considered.

### Triggers

For decades, a prevailing idea has been that when a patient encounters a "trigger," a migraine attack promptly follows.[83–89] As a result, conventional wisdom has been to advise migraine patients to avoid or minimize a myriad of widely believed triggers including certain foods (e.g., chocolate), beverages (e.g., red wine, caffeine), perfumes, soaps, weather changes, sleep deprivation, missed meals, and stress, to name a few.

Yet a universally accepted description of trigger remains elusive. Indeed, IHS does not define "trigger."[28] Moreover, recent research and other scientific scrutiny refutes many long-held beliefs about triggers, demonstrating that little to no correlation exists between the presence or absence of a certain foods, beverages, or other items and an attack's onset.[84–90] Thus, clinicians should cease pre-emptively counseling patients to avoid or minimize the long list of triggers; such recommendations may yield few, if any, benefits.

Instead, clinicians should encourage patients to maintain a headache diary; at least 1 month's information from a headache diary is validated as an effective, accurate migraine diagnosis and treatment assessment tool.[91,92] Diaries of several months' duration can offer further insight into a patient's migraine attack patterns, responses to therapy, and improve communication between clinicians and patients about treatments' benefits. In years past, paper diaries were most common, but today apps downloaded to computers, cell phones, or other electronic devices (including wearable body monitors) can facilitate efficiently gathering diary information. Pharmacists should inquire about diaries' information and review the data with patients.

Importantly, diaries are the best tool to identify patient-specific factors that may be contributing to attacks' onset or increased frequency or duration. If and when diary information illuminates that a particular food, beverage, activity (e.g., extended work hours), deficiency (e.g., sleep), body function (e.g., menstruation), or other identifiable factor is associated with attacks' onset, then efforts to avoid, minimize, or better manage that particular issue are warranted. Moreover, since the gathered information is patient-specific, that individual's motivation to implement changes may be greater compared to when a clinician simply offers a recommendation that is not patient-specific.

### Nondrug and acute migraine therapies

Overall, migraine care goals include[67]:

1. Establish a diagnosis.
2. Educate the patient about their illness and its treatment.
3. Set realistic expectations (e.g., migraine is managed, not cured).
4. Create a formal management plan.
5. Avoid precipitating causes identified via patient diaries.

While medications remain treatment mainstays, nonpharmacologic options can be used for acute or prevention purposes in synergy with or in lieu of medications.[67] Nondrug options should be maximized when drugs have been habitually ineffective or not tolerated, when patients express a preference for nondrugs due to cost or other considerations, or when medications are best avoided such as during pregnancy. Several nondrug treatments have robust evidence of efficacy, few if any AEs, or minimal cost (e.g., biofeedback).

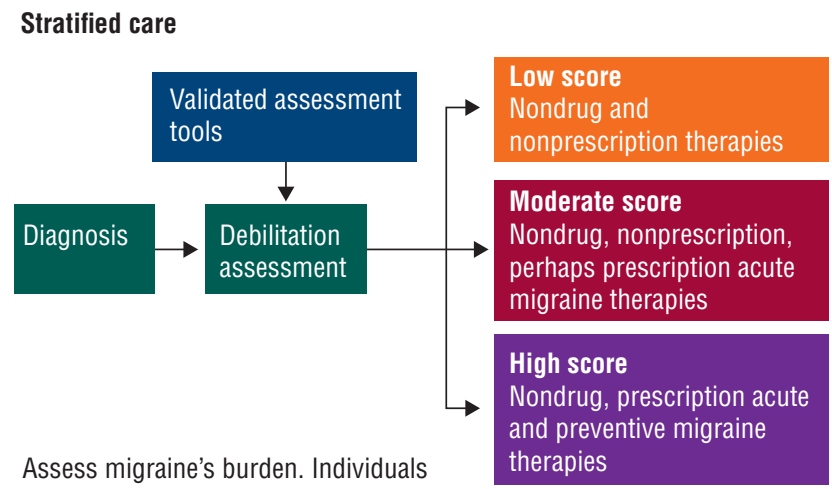
FDA has cleared several neuromodulator devices for acute and preventive treatment; reviewing these devices is beyond this article's scope, but pharmacists can obtain information elsewhere.[67,93]

Acute treatments' goal, stated simply, is to return individuals to their daily activities. Stated more specifically, acute treatment goals are[67]:

1. Rapid and consistent freedom from pain and associated symptoms without recurrence.
2. Restored ability to function.
3. Minimal need for repeat dosing or rescue medication.
4. Optimal self-care and reduced subsequent use of resources (e.g., emergency department visits).
5. Minimal or no AEs.

AHS endorses a stratified care treatment paradigm (Figure).[94] This means that a patient's migraine burden is assessed via a PROM such as MIDAS or HIT-6. Individuals with a low migraine burden, such as MIDAS Grade I, are suitable for nonspecific migraine options such as OTC agents, whereas those with a higher burden are prescribed migraine-specific acute

**Figure.** Stratified care



therapies such as gepants, triptans, or dihydroergotamine.

Stratified care stands in contrast to the treatment approach historically used, step care, in which all patients begin with nonspecific drugs regardless of their burden and those with inadequate responses can then "step up" to migraine-specific therapy. Research demonstrates stratified care's superiority to step care in terms of providing more effective relief.[95]

Pharmacists can take several actions to help patients meet AHS' acute goals. Teach patients an early intervention strategy: the moment an attack commences is the moment to take acute action.[94] Clinical trial data demonstrate improved outcomes when acute medications are consumed at an attack's onset, when symptoms are mild and their duration has been brief. Data also suggest improved medication tolerability with early intervention. Unfortunately, most patients wait to consume an acute medication until after an attacks' symptoms have intensified.[96] Reasons for delaying include usually futile hopes that the attack will cease, wanting to avoid AEs, or "saving" the medication due to cost considerations.

Pharmacists should help patients obtain non-oral therapies when appropriate. Nausea and vomiting are IHS migraine diagnostic criteria because the majority of individuals will experience these unpleasant issues with some, if not all, of their attacks.[28] Non-oral options such as injections, nasal sprays, or suppositories should be offered to people experiencing nausea and vomiting. Also, people experiencing attacks that progress from mild or moderate to severe intensity quickly (generally regarded as <2 hours) are candidates for faster-acting non-oral options.

In clinical practice, subtherapeutic doses and lack of or delayed redosing remain issues. Addressing these issues should be a priority for pharmacists because suboptimal therapy is associated with episodic migraine evolving toward a chronic, refractory-to-treatment headache pattern.[97] Pharmacists should help optimize doses toward the recommended maximum single dose and ensure repeat doses occur at the recommended time. For example, the maximum recommended 24-hour dose of oral sumatriptan is 200 mg. Unfortunately, in practice many people are prescribed a 50-mg dose; a 100-mg dose could provide better efficacy. Most oral and nasal acute migraine medication doses are repeated in 2 hours if needed, whereas most injectable drugs are repeated in 1 hour if needed. Experience in clinical practice shows these differences can sometimes lead to patient confusion as to the proper time to redose a particular drug, while other people wait many hours to retake the dose. These issues could be resolved via a pharmacist's medication counseling.

Table 3 lists AHS' "established efficacy" drugs.[67] Medications of a "Probably Effective" level can successfully be used for many individuals. Still, these drugs are best suited for when adequate trials of established efficacy drugs are ineffective, not tolerated, or when some other patient-specific issue excludes their use.

Every individual with migraine should have at least two acute therapies at their disposal, since no acute treatment has been demonstrated effective for 100% of attacks.[67] Ideally, these options would consist of more than one route of administration. Pharmacists encountering a person with just one acute medication option should help that person attain a second option for use in instances when the first option fails to relieve an attack.

**Table 3.** American Headache Society–endorsed acute medications

| Established efficacy | Probably effective |
|---|---|
| Triptans* (sumatriptan, rizatriptan, zolmitriptan, naratriptan, almotriptan, eletriptan, frovatriptan) | Ergotamine* |
| Dihydroergotamine* | NSAIDs (flurbiprofen, ketoprofen, ketorolac) |
| Gepants* (ubrogepant, rimegepant) | Intravenous magnesium |
| Lasmiditan* | Isometheptene compounds |
| NSAIDs (aspirin, celecoxib oral solution, diclofenac, ibuprofen, naproxen)**,# | Antiemetics |
| Combination acetaminophen/aspirin/caffeine*,# | — |

*FDA-approved.
**Some drugs in this class are FDA-approved.
#Some drugs for mild to moderate migraine.

**Patient scenario *continued***

JW followed through on your recommendation to make an appointment with a physician. She returns to your pharmacy several weeks later, stating that she now keeps a diary, has stopped ibuprofen, and has two acute medication options. Although her acute drugs are normally helpful, yesterday they were ineffective and she missed work. She asks whether you recommend that she seeks a preventive drug.

Migraine attacks vary in terms of elapsed time between the first inkling of an attack and escalation to moderate or severe intensity, duration, presence or absence of associated symptoms, response to treatment(s), and recurrence. Additionally, a person's treatment needs can vary from attack to attack. For example, a person who feels a migraine is coming minutes before delivering an important presentation to work colleagues needs a treatment providing rapid relief with few AEs that could impact their ability to function; an injection or nasal spray are options. In contrast, a person who feels signs of an incoming attack while at home just prior to going to bed for the evening has flexibility in terms of relief onset or tolerability; an oral medication is an option. These two scenarios illustrate why empowering patients with multiple acute treatment choices is essential.

## Preventive therapy

While every migraine patient should have at least two acute options, not every patient requires preventive options. Migraine prevention should be considered for[67,69]:

1. Attacks significantly interfere with patients' daily routines despite acute treatment.
2. Frequent attacks.
3. Contraindication to, failure, or overuse of acute treatments.
4. Patient preference.

In clinical practice, the definition of "frequent attacks" can vary. To help better define this term, AHS published guidance of when to prescribe newly approved preventive medications (Table 4).[67,69] Their recommendation incorporates the use of the MIDAS and HIT-6 PROMs, further illustrating how these tools can guide clinical practice.[67,69]

Table 5 lists the preventive medications endorsed by AHS guidelines.[67,69] The goals of preventive therapies are:

1. Reduce attack frequency, severity, duration, and disability.
2. Improve responsiveness to and avoid escalation in use of acute treatment.
3. Improve function and reduce disability.
4. Reduce reliance on poorly tolerated, ineffective, or unwanted acute treatments.
5. Reduce overall cost associated with migraine treatment.
6. Enable patients to manage their own disease to enhance a sense of personal control.
7. Improve health-related quality of life.
8. Reduce headache-related distress and psychological symptoms.

Key prescribing and counseling points for conventional preventive medications include starting at a low dose and titrating upwards, taking them daily, and allowing an adequate trial of at least 8 weeks.[67] For trying new CGRP mAbs and gepants, a trial should be at least 3 months when administered monthly or 6 months when administered quarterly. A preventive medication can be considered effective if any of the following occur:

1. Fifty-percent reduction in the frequency of days with headache or migraine.
2. Significant decrease in attack duration as defined by the patient.
3. Significant decrease in attack severity as defined by the patient.
4. Improved response to acute treatment.
5. Reduction in migraine-related disability and improvements in functioning in important areas of life.
6. Improvements in health-related quality of life (assessed via PROMs) and reduction in psychological distress due to migraine.

**Table 4.** American Headache Society guidance on prescribing preventive medications

| Prevention should be | Headache days per month | Degree of disability per validated assessment tool[a] |
|---|---|---|
| Offered | 6 or more | None |
| | 4 or more | Some |
| | 3 or more | Severe |
| Considered | 4 or 5 | None |
| | 3 | Some |
| | 2 | Severe |

[a]Such as MIDAS, HIT-6, or Migraine Physical Function Impact Diary.

**Table 5.** American Headache Society–endorsed migraine preventive medications

| |
|---|
| **Episodic migraine**<br>**4 to 14 monthly migraine days and at least moderate disability (MIDAS score of ≤11 or HIT-6 score of ≤50)** |
| Calcitonin gene-related peptide monoclonal antibodies or gepants: erenumab*, fremanezumab*, galcanezumab*, eptinezumab*, atogepant*, rimegepant* |
| Antiseizure: divalproex*, topiramate* |
| Beta-blocker: propranolol*, timolol*, metoprolol, atenolol, nadolol |
| Tricyclic antidepressant: amitriptyline, nortriptyline |
| Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine |
| Candesartan |
| **Chronic migraine**<br>**15 or more monthly headache days** |
| All episodic migraine medications except rimegepant |
| OnabotulinumtoxinA* |

*FDA-approved.

## Conclusion

Pharmacists remain well-positioned to help improve migraine's underdiagnosis and less-than-optimal treatment, particularly by identifying individuals appropriate for OTC medications versus those in need of a physician's referral and prescription therapies. A variety of validated, easy-to-use tools can screen for migraine and assess treatments' benefits. In recent years, FDA approved several acute and preventive medications with novel mechanisms of action that target migraine pathophysiology; these drugs and other guideline-endorsed therapies should be preferred treatments. Every person with migraine should be encouraged to keep a headache diary, which remains the best method to identify patient-specific factors that may be contributing to attacks.

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# CPE Assessment

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

**1. To assess how headaches currently impact JW's life, you should recommend:**
   a. That she get a head X-ray at a local emergency department.
   b. That JW complete a validated assessment tool such as MIDAS or HIT-6.
   c. That you should speak to her boss for input.
   d. That she rate her current pain on a 10-point scale.

**2. You should recommend that JW seek a physician's evaluation because:**
   a. She is experiencing daily headaches.
   b. She is experiencing debilitation (unable to work).
   c. Her ibuprofen consumption constitutes overuse, which can contribute (and for JW likely is contributing) to worsening headaches.
   d. All of the above.

**3. To help identify factors that may be contributing to her headache attacks, JW should:**
   a. Maintain a headache diary.
   b. Skip all meals for 24 hours.
   c. Eliminate chocolate, alcohol, caffeine, and monosodium glutamate from her diet.
   d. None of the above.

**4. She asks which acute medication that you recommend for her. You respond:**
   a. Hydrocodone with acetaminophen, since migraine causes pain, hydrocodone works great for pain, and hydrocodone has no risks of AEs.
   b. She is a poor candidate for OTC drugs; thus, she should seek a physician's consultation.
   c. Switch to acetaminophen 1,000 mg as needed up to four times daily.
   d. Switch to naproxen 500 mg as needed up to three times daily.

**5. Per AHS recommendations, JW is a candidate for migraine preventive medications because:**
   a. She has headaches more than 15 days per month.
   b. She has no comorbid illnesses.
   c. She is over 18 years old.
   d. She lacks insurance coverage.

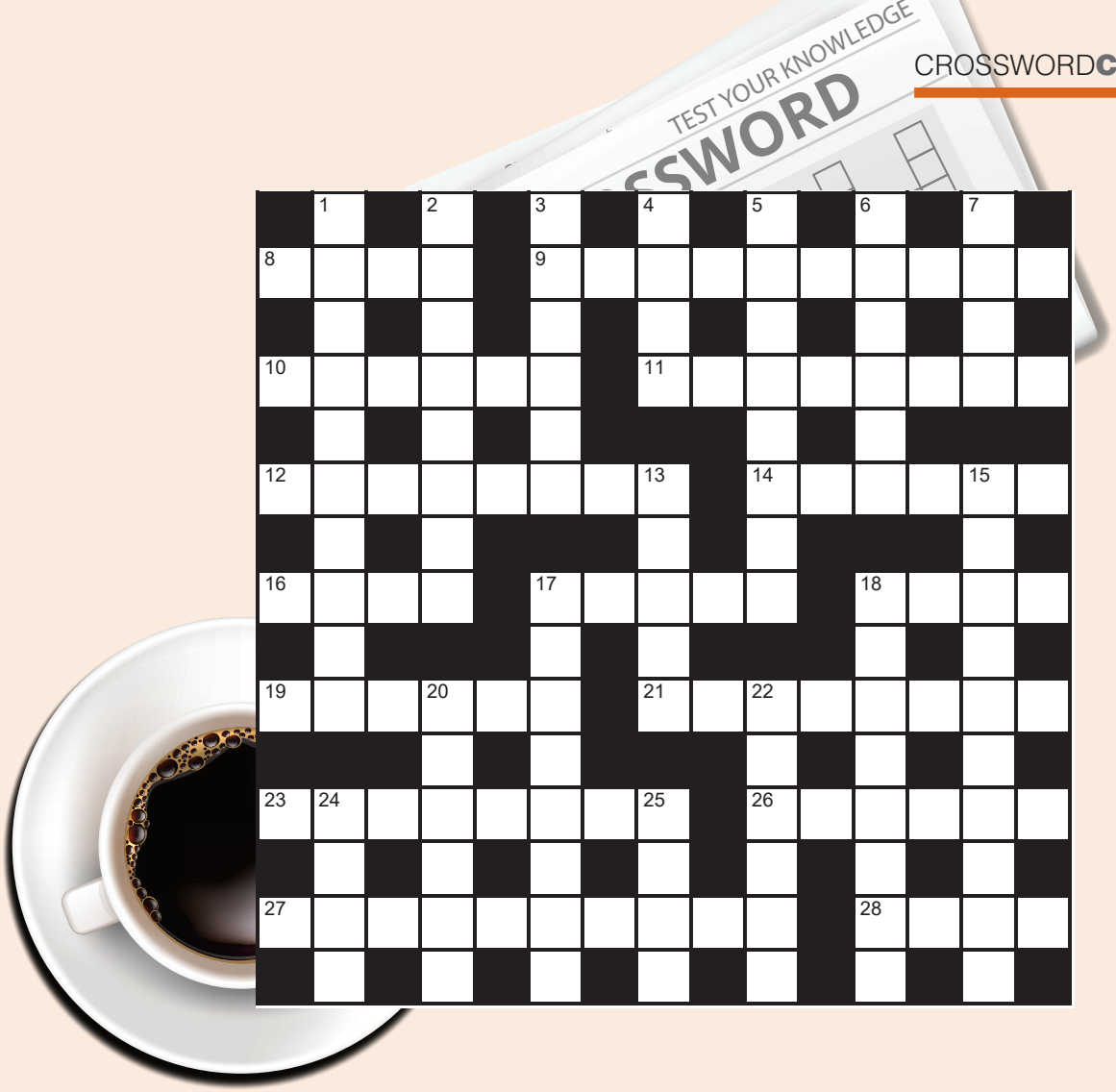
**6. Preventive medication options endorsed by AHS that should be considered for JW include:**
   a. Either ereunumab, fremanezumab, galcanezumab, or eptinezumab ONLY IF she first fails trials of doxepin and paroxetine.
   b. Either ereunumab, fremanezumab, galcanezumab, eptinezumab, atogepant, or rimegepant.
   c. Protriptyline or doxepin.
   d. Oxycodone.

**7. Nonpharmacological migraine treatments endorsed by FDA or guidelines that you should suggest for JW to pursue include:**
   a. At least 10 hours of sleep every evening.
   b. Scented candles.
   c. Neuromodulator devices.
   d. At least eight glasses of water daily.

**8. JW's physician prescribes erenumab. Two days after her first dose, she complains to you that her MIDAS score has not decreased. You should:**
   a. State that a trial of CGRP mAbs such as erenumab should be at least 3 months; hence, 2 days is too soon to assess benefits.
   b. Suggest calling her physician and request a different drug.
   c. Recommend that she increase her ibuprofen dose.
   d. Suggest she find a different doctor.

**9. Goals of JW's erenumab preventive treatment goals include:**
   a. Reducing attack frequency, severity, and duration.
   b. Increasing her appetite and food intake to counteract the days when she has nausea and cannot eat.
   c. Only using erenumab until she can be switched to a daily oral medication.
   d. Treating her comorbidities.

**10. IHS migraine diagnostic criteria state that:**
   a. Head pain must always be unilateral.
   b. Nausea must always be present.
   c. Head pain must always be pulsating.
   d. None of the above.




## Across

**8** Long, for short
**9** Plant oil used in throat lozenges
**10** Roof of the mouth
**11** Mild form of seborrheic dermatitis on the scalp
**12** Tretinoin, for example
**14** With 20 down, may benefit from some psychedelic agents
**16** Org. that credentials pharmacy technicians
**17** Reproductive gland
**18** Blood donation unit
**19** Caused by a lack of healthy red blood cells
**21** Nasal symptom associated with a cold or flu
**23** Type of trial used to test drugs before they come onto the market
**26** Free
**27** Amounts owed by a patient when purchasing an insurance-covered medication or service
**28** Vaping device, for short

## Down

**1** Commonly used medicine for nerve pain
**2** Biotin, thiamine, and riboflavin, among others
**3** Prefix meaning "different"
**4** Acetic, amino, or ribonucleic _____
**5** Reacted to the sight of a needle, maybe
**6** Ancient military hub
**7** Key part of a sphygmomanometer
**13** Bone marrow offerer
**15** NSAIDs and physical therapy can help this
**17** Eye condition that can be treated with latanoprost
**18** Apes
**20** See 14 across
**22** Swallow
**24** Restrooms, in London
**25** Curved structure behind the pupil

Solution is available online at pharmacytoday.org.