Pharmacy Today
An official publication of the American Pharmacists Association
APRIL 2024

CONTINUING PHARMACY EDUCATION
CPE
New Therapeutic Agents Marketed in 2023: Part 1

GENDER-AFFIRMING CARE

PAIN MANAGEMENT
Gabapentin use climbing

HORMONAL CONTRACEPTIVES
Expanded access and options

PHARMACISTS EMBEDDED IN A NEUROLOGY CLINIC
A roadmap for expanded pharmacy services

APhA

BulletinToday

FDA warns patients not to use smartwatches or smart rings to measure blood glucose levels

FDA released a safety alert in February 2024 warning patients about the dangers of smartwatches or smart rings that claim to gauge blood glucose levels without requiring the user to pierce their skin.

Dozens of these models have flooded the market, and none are sanctioned by FDA. The agency said they can produce inaccurate readings with the potential to create harm.

Armed with the wrong information, people with diabetes may adjust their medication and end up putting themselves at risk. Taking too much insulin, sulfonylureas, or other treatment can drive blood glucose to dangerously low levels that can escalate quicky to mental confusion, coma, or even death.

For patients who rely on accurate blood glucose measurements to manage their disease, health care providers can point them to appropriate FDA-authorized devices.

Data from authorized devices may be transferred and displayed via applications on some smartwatches or smart rings, which FDA clarifies are not the target of its safety communication. Their warning applies only to unauthorized devices that claim to actually measure blood glucose through noninvasive methods. ■

Survey looks at characteristics of young adults who use e-cigarettes

In 2021, roughly 31% of adults in the United States aged 18 to 24 years reported ever having used an electronic nicotine product, according to new research from HHS' Agency for Healthcare Research and Quality (AHRQ).

Among other age groups, the prevalence of having ever used an electronic nicotine product was about 25% of adults aged 25 to 34 years, 18% of adults aged 35 to 44 years, 11% of those aged 45 to 64 years, and 4% of those aged 65 and older.

The data come from the AHRQ's 2021 Medical Expenditure Panel Survey Household Component.

Overall, roughly 30% of young adults living in metropolitan areas reported ever having used an electronic nicotine product, while the rate for young adults living outside of metropolitan areas was 39%. Young adults in excellent health were less likely to report ever having used an electronic nicotine product compared with young adults in fair or poor physical or mental health, the survey found.

Additionally, ever use of an electronic nicotine product was more common among adults who smoked or had an asthma diagnosis compared with those who did not smoke or have a diagnosis of asthma. ■

CDC: Older adults should get another COVID-19 dose this spring

A February 2024 meeting of CDC's ACIP ended with a recommendation—which CDC Director Mandy Cohen, MD, accepted—that U.S. adults aged 65 years and older "should" get a second dose of the updated COVID-19 vaccines.

The latest vaccine formulations from Pfizer-BioNTech, Moderna, and Novavax were introduced in the fall of 2023 and reportedly are 40% to 50% effective against symptomatic COVID-19 infection and hospitalization.

Data shared by federal researchers at the ACIP meeting revealed that adults who were immunized with the newest vaccines represented just 4% of COVID-19–related hospital admissions in October and November versus 25% for adults who were boosted the previous fall but did not receive the newest vaccine versions last year.

The call for second doses this spring applies only to older Americans, with adults aged 18 to 64 years less likely to develop acute illness or require hospitalization, and to people who are immunocompromised. ■

BP improves with patients taking GLP-1, says study

Results from a recent study published in the American Heart Association's *Hypertension* showed that the GLP-1 tirzepatide reduced 24-hour systolic BP both at night and in the daytime compared with placebo.

Researchers examined the impact on ambulatory BP from tirzepatide, which was shown during a large clinical trial to lower BP readings taken at the doctor's office. As a preplanned substudy to the SURMOUNT trial, 1,600 participants with obesity but not T2D (tirzepatide is approved to treat both) underwent ambulatory BP monitoring for 24 hours at baseline and again at week 36.

All patients had a body mass percentage indicating overweight or obesity, BP higher than 140/90 mm Hg, and, if taking antihypertensive therapy, the same regimen in place for at least 3 months. Each patient received either one of three doses of tirzepatide or placebo. The final analysis included 494 participants who had valid ambulatory BP monitoring data at baseline and week 36.

Based on mediation analyses, the improvement was attributed in part to reduced weight. While participants also experienced an acceleration in heart rate, the evidence suggests this outcome likely would abate with continued treatment over the long term.

"This study demonstrates that tirzepatide improves 24-hour BP in obesity-related hypertension," the study authors wrote. "While being consistent with in-office measurement, the current study uses a method that is superior to office BP alone for predicting cardiovascular risk." ■

Low-dose aspirin during pregnancy appears to have no effect on child's neurodevelopment

Low-dose aspirin during pregnancy is safe, according to a new study published in the American College of Obstetricians and Gynecologists' *Obstetrics and Gynecology*. Researchers found that the Bayley Scales of Infant and Toddler Development (Bayley-III) cognitive composite scores indicated no difference when pregnant patients took low-dose aspirin early in pregnancy compared to a placebo. In other words, it neither worsened nor improved a child's neurodevelopment.

The research was a follow-up study to the multinational ASPIRIN trial, which showed that when women were randomized to low-dose aspirin during pregnancy, they had lower rates of preterm birth, preterm hypertensive disorders, and perinatal mortality. Researchers of the current study wanted to gather additional information on any potential long-term effects of in utero aspirin on a child's neurodevelopment later. Children were assessed at age 3 years with both Bayley-III and the ASQ-3 (Ages and Stages Questionnaire, 3rd edition).

A total of 640 children (329 in the low-dose aspirin group, 311 in the placebo group) were evaluated between September 2021 and June 2022. Mothers were randomized to daily low-dose aspirin (81 mg) or placebo through early pregnancy up to 37 weeks.

No significant differences were seen in the language composite score or the motor composite score. Authors wrote that communication, gross motor, fine motor, problem-solving, and personal–social components of the ASQ-3 did not differ between groups either. Researchers also noted maternal characteristics, delivery outcomes, breastfeeding rates, breastfeeding duration, and home environment and also found no differences. ■

Age-related risk of serious falls increases with opioid use

New research published in *JAMA Internal Medicine* shows that opioid analgesics elevate the likelihood of falls in all adult patients, but the greatest risk is among individuals aged 85 years and older.

The retrospective population-based study included more than 3 million Australians who initiated prescription opioid treatment from 2005 through 2018 in New South Wales.

Patients across the age spectrum were most in danger of falling within the first 28 days of the opioid exposure period. Overall, more than 506,500 serious falls were documented during the study period, including 5,210 resulting in death.

The incidence of serious falls was highest among older adults, underscoring the need for additional fall prevention measures in a population who is already vulnerable due to frailty, polypharmacy, and other factors.

The study authors also emphasized that more needs to be done in terms of prevention education and strategies for younger adults. These individuals are at risk because of fewer former exposures at baseline and higher doses.

Prescribers should carefully weigh the risks and benefits before initiating an opioid regimen, the investigators conclude, especially if patients have pre-existing risk factors—such as older age—or if the plan is to give them high daily doses.

"Targeted falls prevention efforts may be most effective within the first month following opioid initiation," the authors wrote. ■

Pennsylvania pharmacists can now bill Medicaid for pharmacy services

In Pennsylvania, Medicaid now recognizes pharmacists as providers. Effective March 1, 2024, pharmacists can enroll as providers and bill for pharmacy services.

"This recognition underscores the crucial role pharmacists play in health care delivery, particularly in underserved communities," wrote the National Alliance of State Pharmacy Associations (NASPA) on their website.

The official recognition aligns with Act 80 of 2020 and State Board of Pharmacy regulations, granting pharmacists provider status and allowing them to bill Pennsylvania Medicaid for rendered services.

To be paid for services in an outpatient setting, pharmacists will need to enroll with Pennsylvania's Medicaid program and individual Managed Care Organizations. The Pennsylvania Department of Human Services will offer training sessions for pharmacists interested in enrolling as billing providers.

"PA Medicaid's recognition of pharmacists as care providers comes at a critical time when patients are increasingly losing access to needed care in communities, notably those in rural and urban underserved areas where pharmacists are capable, accessible, and passionate about ensuring the health of our communities," said Christopher Antypas, PharmD, president of the Pennsylvania Pharmacists Association.

"This opportunity would not have been possible without Pennsylvania-based pharmacy organizations speaking clearly, with a unified voice," he continued in the press statement. "Your state pharmacy associations are unified in comprehensively advocating for the value of pharmacy care to all stakeholders including the legislature, state agencies, payors, and patients." ■

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CPE

44 New therapeutic agents marketed in 2023: Part 1

Daniel A. Hussar

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Pharmacists play an important role in caring for transgender patients

There is a growing need for pharmacists to provide care for transgender patients. Gender-affirming care and appropriate hormonal treatment are essential steps for individuals who are transitioning to align their appearance with their gender identity. Pharmacists play an important part in helping patients to safely navigate this pathway.

This month's *Pharmacy Today* cover story highlights the role of pharmacists on multidisciplinary teams caring for transgender patients. The need for and the value of pharmacists makes sense in both short- and long-term care for these individuals. Many patients who are transitioning will be on lifelong drug therapy. In the short term, pharmacists can educate patients about their medications and help them gain access to gender-affirming hormonal therapies that may not be covered by insurance.

Patients who are established on a drug therapy regimen continue to rely on their pharmacists. As shown by the authors of a recent article published in *JAPhA*, pharmacists are needed to help manage comorbid conditions that can develop or worsen with long-term hormonal treatment, such as hyperlipidemia or diabetes, and to monitor patients for potential adverse effects.

In this issue of *Today*, you will also find recent new drug approvals, get tips for OTC treatment of muscle pain, and get the latest on prebiotics and their potential benefits. Learn what to watch for as COVID-19 drug therapies transition to the commercial market, and catch up on your CPE credit with this month's article on new therapeutic agents marketed in 2023.

Most transgender patients encounter significant life challenges that extend beyond the scope of medication access and management. Help support your patients who are making this journey by creating a safe and welcoming environment in your pharmacy and affirming their gender identity. For example, using a patient's preferred name and pronouns, and helping your staff to do the same, is an important part of establishing trust and communicating to patients that you respect and value their gender identity.

Have a great *Today*! ■

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The prescription for America's mental health care shortage

Last year, the Commonwealth Fund published an eye-opening report about the significant shortage of behavioral health care providers of all types. Nearly half of all Americans are facing one sort of behavioral health challenge or another in their lifetime—from anxiety disorders to SUDs to mood disorders to a host of conditions in between. Yet for most of us, finding a provider is next to impossible. It takes over 2 months to be seen in-person for an initial psychiatric consult, and nearly a month for a telehealth visit based upon 2023 data. It's unacceptable, and policymakers are doing very little to address the issue.

There are no easy answers because treatment of mental health conditions tends to require the engagement of multiple health professionals—psychiatrists and psychologists, licensed clinical counselors, social workers, nursing professionals, and yes, even pharmacists. The Commonwealth Fund, in identifying the challenges and the opportunities to address workforce shortages, failed to acknowledge the over 1,560 pharmacists with Psychiatric Pharmacy Specialty Certification (BCPP) who provide comprehensive medication management for this population. Thankfully, The National Council for Mental Wellbeing Medical Director Institute and others across the country have recognized that pharmacists are critical to addressing this need. The American Association of Psychiatric Pharmacists (AAPP) brings together these professionals, and APhA is proud to support their efforts to gain greater recognition of the specialty.

Nearly every patient with a psychiatric care need receives treatment with medication as a part of therapy. Medication can be one of the most effective interventions when combined with counseling or behavioral therapy. Yet psychiatric medications can be difficult to manage due to multiple factors—cost of therapy, adverse drug effect profiles, drug interactions—all of which lead to nonadherence to therapy. Pharmacists are medication experts and the team member responsible for appropriate medication therapy outcomes. It's not surprising that studies going back well over a decade have found that pharmacists improve outcomes of therapy in psychiatric care and substantially reduce costs for both the patient and the payer.

No one health care provider can solve the mental health crisis. However, federal and state policymakers are not doing enough. APhA calls upon our profession to join us in advocating for increased incentives for health care providers to pursue careers in behavior health fields, including for pharmacists who choose to pursue specialization in psychiatric care. This could include loan repayment programs. BCPP pharmacists should be recognized as providers under Medicare and by state Medicaid programs so that these well-qualified professionals can be put fully in the game to help address this serious personnel shortage.

HRSA and CMS should provide funding mechanisms to support outpatient clinics, universities, and health-systems establishing and growing postgraduate residency programs in psychiatric pharmacy to increase the number of pharmacists who pursue this career path. Schools and colleges of pharmacy should intensify their promotion of psychiatric pharmacy as an important career pathway. Pharmacists searching for a refresh of their careers should seriously consider preparatory coursework and hands-on training in this field. We could easily double the number of pharmacists with BCPP certification and still have a shortage of pharmacists in this sector.

Finally, all pharmacists should consider training in mental health first aid and include mental health and well-being as a part of this year's continuing professional development plans, such as through pharmacist.com.

For every pharmacist. For all of pharmacy. ■

NEW DRUG

LETIBOTULINUMTOXINA-WLBG
(Letybo—Hugel Inc.)

Drug class: Letybo is a cetylcholine release inhibitor.

Indication: Letybo is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients.

Recommended dosage: The recommended dose is 0.1 mL (4 units) by I.M. injection into each of five sites, for a total dose of 20 units. The dosage form and strength are 50 units or 100 units of freeze-dried powder in a single-dose vial.

Contraindications: Contraindications include known hypersensitivity to any botulinum toxin preparation or to any of the components in the Letybo formulation and infection at the injection site.

Common adverse effects: The most common adverse reaction is headache.

Warnings and precautions: Seek immediate medical attention if respiratory, speech, or swallowing difficulties occur. Potency units of Letybo are not interchangeable with other preparations of botulinum toxin products. If a hypersensitivity reaction occurs, discontinue Letybo and immediately initiate appropriate therapy.

Adverse events have been reported involving the CV system, some with fatal outcomes. Use caution when administering to patients with pre-existing CVD. Concomitant neuromuscular disorder may exacerbate clinical effects of treatment. Use with caution in patients with compromised respiratory function or dysphagia. Coadminister aminoglycoside antibiotics, anticholinergic agents, or any other agents that interfere with neuromuscular transmission with caution, as these may augment the effect of Letybo.

CEFEPIME; ENMETAZOBACTAM
(Exblifep—Allecra Therapeutics)

Drug class: Exblifep is a cephalosporin antibacterial and β-lactamase inhibitor.

Indication: Exblifep is indicated for the treatment of patients 18 years and older with complicated UTIs, including pyelonephritis caused by designated susceptible microorganisms. Exblifep should only be used to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria to reduce the development of drug-resistant bacteria.

Recommended dosage: Exblifep is supplied as a sterile powder for reconstitution in single-dose vials containing 2 grams cefepime and 0.5 grams enmetazobactam. Administer Exblifep 2.5 grams (2 grams cefepime and 0.5 grams enmetazobactam) every 8 hours by I.V. infusion over 2 hours for 7 days to 14 days, in patients 18 years and older with an eGFR between 60 to 129 mL/min. Dosage adjustment is recommended in patients with renal impairment who have an eGFR <60 mL/min or >130 mL/min. See label for a table of recommended dosages based on renal function.

Contraindications: Exblifep is contraindicated in patients with a history of serious hypersensitivity reactions to the components of Exblifep (cefepime and enmetazobactam), or other β-lactam antibacterial drugs.

Common adverse effects: The most frequently reported adverse reactions occurring in ≥5% of patients treated with Exblifep were increased transaminases, increased bilirubin, headache, and phlebitis/infusion site reactions.

Warnings and precautions: Hypersensitivity reactions have been reported in patients treated with Exblifep. Serious and occasionally fatal hypersensitivity reactions, including anaphylaxis, have been reported with β-lactam antibacterial drugs. If an allergic reaction to Exblifep occurs, discontinue the drug and institute appropriate therapy. Neurotoxicity has been reported during treatment with cefepime. Most cases occurred in patients with renal impairment who did not receive appropriate dosage adjustment of cefepime. If neurotoxicity occurs, discontinue Exblifep and institute appropriate supportive measures. *Clostridioides difficile*–associated diarrhea has been reported with nearly all systemic antibacterial agents, including Exblifep. Evaluate if diarrhea occurs.

NEW INDICATION

AMIVANTAMAB-VMJW
(Rybrevant —Janssen Biotech)

Drug class: Rybrevant is a bispecific epidermal growth factor receptor (EGF)–directed and MET receptor–directed antibody.

Indication: Rybrevant is indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with EGF receptor exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.

Recommended dosage: The recommended dosage of Rybrevant is based on baseline body weight and administered as an I.V. infusion after dilution. Administer 350 mg/7 mL (50 mg/mL) in a single-dose vial intravenously per infusion rates listed in the label.

Administer premedications as recommended. Administer Rybrevant via

a peripheral line weekly for 4 weeks, with the initial dose as a split infusion in Week 1 on Day 1 and Day 2, then administer every 2 weeks thereafter.

Contraindications: None.

Common adverse effects: The most common adverse reactions (≥20%) were rash, infusion-related reactions, paronychia, musculoskeletal pain, dyspnea, nausea, fatigue, edema, stomatitis, cough, constipation, and vomiting. The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased albumin, decreased phosphate, decreased potassium, increased alkaline phosphatase, increased glucose, increased gamma-glutamyl transferase, and decreased sodium.

Warnings and precautions: Interrupt infusion at the first sign of infusion-related reactions. Reduce infusion rate or permanently discontinue Rybrevant based on severity. Monitor for new or worsening symptoms indicative of interstitial lung disease and immediately withhold Rybrevant in patients with suspected interstitial lung disease/pneumonitis and permanently discontinue if interstitial lung disease/pneumonitis is confirmed. Rybrevant may cause rash, including acneiform dermatitis and toxic epidermal necrolysis. Withhold, reduce dose, or permanently discontinue Rybrevant based on severity. Promptly refer patients with worsening eye symptoms to an ophthalmologist. Withhold, reduce dose, or permanently discontinue Rybrevant based on severity. Rybrevant can cause fetal harm. Advise patients of the potential risk to the fetus and to use effective contraception.

NEW FORMULATION

CLOBETASOL PROPRIONATE

(Clobetasol propionate—Formosa Pharmaceuticals)

Drug class: Clobetasol is a corticosteroid.

Indication: Clobetasol propionate is indicated for the treatment of postoperative inflammation and pain following ocular surgery.

Recommended dosage: Instill one drop of clobetasol propionate ophthalmic suspension 0.05% into the affected eye twice daily beginning the day after surgery and continuing throughout the first 2 weeks of the postoperative period. Wash hands well before each use.

Contraindications: Most active viral diseases of the cornea and conjunctiva, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also mycobacterial infection of the eye and fungal diseases of ocular structures are included in contraindications.

Common adverse effects: Ocular adverse reactions occurring in ≥1% of subjects in clinical studies who received clobetasol propionate ophthalmic suspension 0.05% included eye inflammation (2%), corneal edema (2%), anterior chamber inflammation (2%), cystoid macular edema (2%), intraocular pressure elevation (1%), photophobia (1%), and vitreous detachment (1%). Many of these reactions may have been the consequence of the surgical procedure.

Warnings and precautions: Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve and defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored. Prolonged use of corticosteroids may result in posterior subcapsular cataract formation. The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy, and when appropriate, fluorescein staining. Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated. Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate. ■

FDA approves first OTC glucose monitor

On March 5, 2024, FDA cleared the first OTC continuous glucose monitor (CGM) for marketing, allowing adults to purchase the CGM without a prescription. The Dexcom Stelo Glucose Biosensor System is an integrated CGM (iCGM) intended for patients 18 years and older who do not use insulin, such as individuals with diabetes treating their condition with oral medications, or those without diabetes who want to better understand how diet and exercise may impact blood glucose levels. Importantly, this system is not for individuals with problematic hypoglycemia, as the system is not designed to alert the user to this potentially dangerous condition.

The Stelo Glucose Biosensor System pairs a wearable sensor with an application installed on a user's smartphone or other smart device to continuously measure, record, analyze, and display glucose values. Users can wear each sensor for up to 15 days before replacing with a new sensor. The device presents blood glucose measurements and trends every 15 minutes in the accompanying app. Users should not make medical decisions based on the device's output without first consulting their health care provider.

Adverse events included local infection, skin irritation, and pain or discomfort. ■

Muscle aches and pain

Mary Warner

Everyone experiences muscle pain (myalgia) at some point in their lives, whether due to overexertion, injury, or disease. Fortunately, numerous options, including rest, massage, and medications, are available to relieve the pain.

The most common type of muscle pain is caused by overexertion, repeated unaccustomed muscle contraction, usually from sports or other exercise. Muscle soreness is delayed, usually by 8 hours or more, and generally peaks at 24 to 48 hours but can last for days. Overexertion pain is common among people who don't exercise regularly but then begin an exercise regimen at a level of high intensity. Tension or poor posture can also produce this type of muscle pain.

Pain resulting from injury or trauma to the muscle, whether from overuse or an unexpected pull or twist, is often sharper and more troublesome than the pain from simple overexertion and takes longer to resolve, often becoming chronic.

Finally, myalgia can result from systemic infections (e.g., the flu), chronic disorders (i.e., fibromyalgia or lupus), or medications, including ACE inhibitors and statins.

Nonpharmacological relief

Probably the most common method of treating muscle pain without medication is the RICE method—rest, ice, compression, and elevation—which helps to reduce swelling, ease pain, and speed up healing. Patients should rest the affected body part and apply ice for the first 24 to 72 hours after injury to reduce inflammation. After that, heat often feels more soothing.

Muscle aches from overuse and fibromyalgia often respond well to massage and gentle stretching as well. Somewhat counterintuitively, exercise can help restore proper muscle tone, but it's important, as always, to begin slowly and warm up completely before exercising.

Medication relief

If these nonpharmacological methods don't work, patients can take nonprescription medications to relief muscle aches and pains. Systemic analgesics such as acetaminophen and NSAIDs (e.g., aspirin, ibuprofen, naproxen, and magnesium salicylate tetrahydrate) are most commonly used as initial treatment for muscle pain. It's important to note that because chronic use of NSAIDs can lead to severe adverse effects, including GI bleeding and increased risk of CVD, systemic analgesic use should be limited to 10 days and patients should see their primary care provider if pain continues past this time.

Although systemic analgesics are often chosen as the initial treatment of muscle pain, there is evidence that topical analgesics may be more effective while limiting adverse effects. Options include creams, patches, and gels containing menthol (e.g., Aspercreme, Bengay, Icy Hot), lidocaine (e.g., Aspercreme, Salonpas), trolamine salicylate (e.g., Sportscreme, Aspercreme), and diclofenac sodium (e.g., Voltaren). Products containing combinations of methyl salicylate, menthol, lidocaine, and/or camphor are also widely available.

Recommended dosage for muscle pain relief

Medication	Dosage forms	Usual adult dosage (maximum daily dosage)
Acetaminophen	Immediate-release, extended-release, effervescent, dispersible, and chewable tablets; capsules; liquid; suppositories; powder packet	325–1,000 mg every 4–6 hours as needed for immediate-release products (4,000 mg); 650–1,300 mg every 8 hours as needed for extended-release products (4,000 mg)
Ibuprofen	Immediate-release and chewable tablets, capsules, suspension	200–400 mg every 4–6 hours as needed (1,200 mg)
Naproxen sodium	Immediate-release and delayed-release tablets, capsules	220 mg every 8–12 hours as needed (660 mg). For initial dose: 2 tablets within the first hour
Aspirin	Immediate-release, buffered, enteric-coated, film-coated, effervescent, and chewable tablets; suppositories	325–1,000 mg every 4–6 hours as needed (4,000 mg)
Magnesium salicylate	Tablets	1,160 mg every 6 hours as needed (4,640 mg)

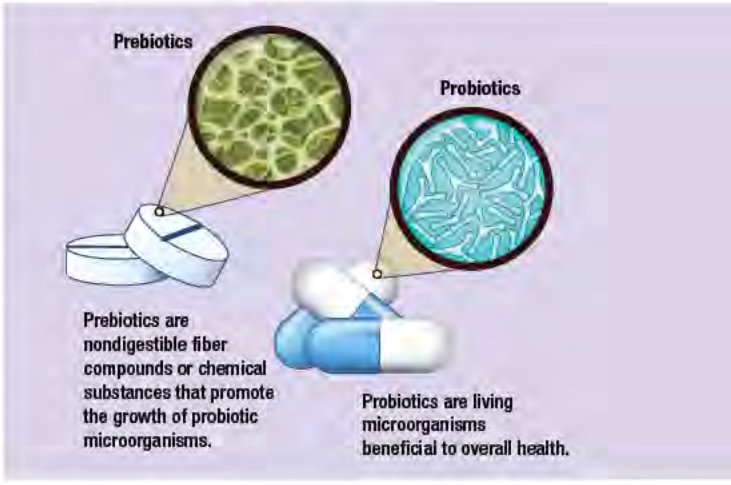
What to tell your patients

Advise patients that if muscle aches are a result of a specific disease or condition, the underlying condition should be treated first, with pain relief as a secondary concern. If muscle pain is severe, lasts for more than 10 days, is related to starting or changing doses of an ACE inhibitor or statin, or if swelling or redness is visible around the affected muscle, patients should consult their primary care physician. Also advise patients to limit use of NSAIDs to dosages needed to relieve pain rather than routine use. ■

Prebiotics: A gut check

Mickie Cathers

Prebiotic dietary supplements boast that they promote digestive health, reduce inflammation, increase energy and drive, and may help with appetite control. All this and they're also vegan, gluten-free, sugar-free, and keto-friendly. What are prebiotics, anyway?



Background

Prebiotics and probiotics are not the same thing. Probiotics contain live microorganisms meant to maintain or improve normal microflora (i.e., gut bacteria). Prebiotics act as food for gut bacteria and improve the balance of microorganisms. While probiotics are found in foods such as yogurt and sauerkraut, prebiotics are found in typically high-fiber foods including whole grains, asparagus, artichoke, bananas, garlic, onions, and soybeans. Most prebiotic compounds are dietary fibers or other carbohydrates including inulin, fructooligosaccharides, galactooligosaccharides, and lactulose.

Prebiotics act as food for gut bacteria and improve the balance of microorganisms.

Due to the lack of enzymes in our intestines that hydrolyze the polymer bonds of prebiotics, these dietary fibers remain in the GI tract and resist digestion in the small intestine. They reach the colon intact, where they are selectively fermented to produce short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate. These are then absorbed by the intestinal epithelium or transported to the liver, exerting beneficial effects such as regulating immunity, resisting pathogens, improving intestinal barrier function, increasing mineral absorption, and lowering blood lipid levels. The presence of prebiotics in the gut is associated with the production of both protective mucus and anti-inflammatory cytokines. Prebiotics also play a role in the treatment of obesity as SCFAs regulate fat metabolism and are associated with the secretion of satiety hormones, thus preventing overeating.

Is there a benefit?

Research into the relationship between gut microflora and disease is ongoing. A study published on November 22, 2023, in *Food Science & Nutrition* presented results of a randomized, double-blind clinical trial including 92 patients with coronary artery disease. Liu and colleagues evaluated the effects of 8 weeks of coadministration of prebiotic inulin with probiotics on the endocannabinoid system, gut microbial composition, and inflammatory parameters associated with coronary artery disease. Patients were randomly allocated to receive inulin (15 mg/day), *Lactobacillus Rhamnosus* probiotic capsules, or inulin plus probiotic supplements. Results revealed that probiotic–prebiotic cosupplementation significantly decreased serum levels of interleukin-6, toll-like receptor 4, and lipopolysaccharides, while increasing total antioxidant capacity, compared with placebo. Their data provided preliminary evidence that administration of prebiotics with probiotics enhanced and improved the gut barrier, diminished metabolic endotoxemia, and significantly improved the endocannabinoid receptors and inflammatory biomarkers more than either of the two supplementations given alone.

Dosage and availability

Prebiotic supplements are available online and on store shelves in capsules, gummies, and powders, either alone or often in combination with a probiotic product. Prebiotic supplements are mostly just pure fiber extracted from artichoke, acacia, or guar gum and promoted as a daily dose of fiber. These supplements are also sold in travel packets meant to be mixed with 8 oz of a cold beverage or added to a smoothie. Pure inulin powder is also available. Supplement serving sizes range from 3 g to 19 g, while dosages in trials range from 30 g/day to 60 g/day.

Prebiotic supplements are mostly just pure fiber extracted from artichoke, acacia, or guar gum and promoted as a daily dose of fiber.

What to tell your patients

A healthy and balanced diet will already include prebiotics in the form of foods such as bananas, oats, and other high-fiber vegetables. While a prebiotic supplement is unnecessary for most healthy adults, recommend consultation with a health care provider for those patients wishing to add the supplement to their diet. Prebiotic supplements are generally regarded as safe and adverse effects are rare. However, adding high fiber content such as that found in prebiotic supplements too quickly can result in bloating, cramping, or intestinal gas. Advise patients to drink plenty of water with prebiotic supplementation. ■

Use of gabapentin in U.S. shows no sign of slowing

Elizabeth Briand

Gabapentinoid use has continued to climb in the United States, despite a lack of strong evidence for its effectiveness in pain management and other uses, according to a recent study published in the January 2024 issue of the *Annals of Family Medicine*.

Researchers analyzed data from the 2002–2021 Medical Expenditure Panel Survey (MEPS) and showed that the proportion of the population reporting use of a gabapentinoid medication increased from 1.2% in 2002 to 4.7% in 2021. A probability increase was seen for nearly all age groups, with the probability of gabapentinoid use among individuals aged 70 and older at 9%.

"Clinicians strive to avoid opioids and these medications give us a potential alternative, non-opioid treatment."

The study, which is a continuation of a previous MEPS data analysis by Johansen through 2015, noted that gabapentinoids "continue to be commonly used in conjunction with other sedating medications, which is concerning in light of FDA's 2019 warning about co-prescribing of gabapentinoids with other central nervous system depressants."

In assessing the root cause of that finding, Johansen said, "My guess is that it is a function of trying to avoid increasing opioid doses. It is likely akin to using it as an adjunctive medication to opioids. To my knowledge there isn't much evidence to support its use in situations such as this in terms of efficacy or decreasing adverse effects."

Garofoli noted that these medications are typically added within a diverse pain management treatment plan. "In the realm of pain management, various gabapentin formulations are FDA-approved for the treatment of post-herpetic neuralgia, while pregabalin is FDA-approved for treatment of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia, fibromyalgia, and neuropathic pain associated with spinal cord injury."

Gabapentinoids, however, also "have been utilized off-label for a variety of indications beyond those FDA approvals," he said.

The study also sought to examine the likelihood of individuals starting, stopping, or continuing gabapentinoids. The longitudinal analysis looked at the percentage of people still using the medications after 1 year and found that the probability increased until 2016 to 2017, when it plateaued at just over 3%. The data also showed that new use of the medications was more prevalent than discontinuation, especially in the earlier years of the data, but showed the difference declining more recently.

An ongoing trend

Michael Johansen, MD, a family medicine physician with OhioHealth who led the study, said he was unsurprised by the results of this analysis, noting that it was "consistent with what I see in clinical practice."

Mark Garofoli, PharmD, clinical assistant professor at West Virginia University School of Pharmacy in Morgantown, WV, agreed. The results were "completely expected given the tightening of the reins on other pain management medication options such as prescription opioids."

Individuals coping with musculoskeletal pain and diabetes accounted for the highest proportion of the population using gabapentinoids, but patients with other conditions, including polyneuropathies, fibromyalgia, seizure disorder, anxiety disorder, and migraine, were also prescribed the medications.

"We lack effective treatment for many of these chronic pain conditions," Johansen said. "Clinicians strive to avoid opioids and these medications give us a potential alternative, non-opioid treatment."

Providing added support for patients

As the use of gabapentinoids continues, it remains important for physicians and pharmacists to work with patients and reassess the necessity of these medications on a routine basis, said Johansen. He said it's crucial for clinicians to recognize that these medications are rarely a solution to chronic pain conditions and carry the potential for a number of adverse effects.

The ongoing trends in gabapentinoid use can serve as a reminder that "pain management guidelines need to look at the whole picture and not just one type of medication," said Garofoli. "In other words, if we recommend reserving, or actually limit, one pain medication (opioids), another will take its place."

Garofoli said the observed increase in gabapentinoid prescription medications utilization propels pharmacists to another opportunity for providing patient care in the form of patient counseling. "Although OBRA '90 requires the offering of patient counseling, the core of our being as pharmacists should propel an automatic conversation, always," he said. ■

Barriers still present for OUD medications even after passage of MAT Act

Parth Patel, PharmD

Even after passage of the Mainstreaming Addiction Treatment (MAT) Act in late 2023, patients still face difficulty gaining access to buprenorphine—the gold standard for treating patients with OUD.

The MAT Act eliminated the need for prescribers to register and fill out the X-waiver, which served as a system to control the number of providers who could prescribe buprenorphine.

Currently, 10 states allow pharmacists to prescribe controlled substances. Upon passage of the MAT Act, pharmacists in these states have the ability to prescribe buprenorphine to patients with OUD depending on CPAs and the pharmacist's practice setting within their respective state. With the X-waiver requirement removed, all physicians will be able to prescribe buprenorphine, but other health care providers who don't have full prescriber status can only prescribe if their state allows it. For pharmacists, this only affects those in the 10 states that allow them to prescribe buprenorphine.

While the passage of the MAT Act has efficiently eliminated one barrier affecting patients' ability to gain access to buprenorphine, there is no evidence that more patients are being treated with the medication.

During a November 2023 APhA Pulse on Practice Presentation, Josh Bolin, associate executive director of government affairs and innovation at the National Association of Boards of Pharmacy (NABP), stated that one of the main reasons for not seeing an increase in buprenorphine prescribing from all health care providers, including pharmacists, is due to a "lack of awareness and stigma."

Bolin said that providers are focused on taking care of patients and may not be aware of the changes in federal legislation that would allow them to prescribe this FDA-approved medication.

Stigma

Stigma associated with seeking treatment and caring for patients who have OUD is a limiting factor, and resources must be created to help prescribers feel confident in helping patients suffering from OUD, noted speakers during the Pulse on Practice presentation.

> One way to fight the stigma associated with OUD is to "continue to push education and understanding...that buprenorphine is safe."

Elizabeth Connolly, assistant director of the Public Health Office of National Drug Control Policy, said that one way to fight the stigma associated with OUD is to "continue to push education and understanding...that buprenorphine is safe."

Bolin responded that NABP and APhA are collaborating with various colleges of pharmacy to create a multiperspective consensus-based practice guideline that pharmacists can use as a resource to help guide their decisions in the treatment of OUD.

Bolin said the creation of this resource could help pharmacists confidently make decisions for their patients who would benefit from buprenorphine and other FDA-approved medications for OUD treatment. Methadone and naltrexone are also FDA-approved for this purpose.

Barriers at the pharmacy

Stigma and prescribing hesitancy are not the only barriers patients are currently facing when trying to obtain buprenorphine, however. Patients are going to pharmacies with valid prescriptions, but due to limits on how much buprenorphine is being supplied to pharmacies, they are still unable to obtain their prescriptions.

When asked why patients who are prescribed buprenorphine are still having issues getting access to medications at the pharmacy counter, Matthew Strait, deputy assistant administrator at DEA's Office of Diversion Control Regulatory, said that the issue is complex because drug distributors set the amount of medications they send to pharmacies, and the only requirement from DEA is that each distributor has a system in place to report suspicious activity.

Despite the expected increase in buprenorphine shipping, many drug distributors seem to be apprehensive about increasing the amount of stock they send to pharmacies because of worries about the increase in supply appearing suspicious to DEA.

Strait said that DEA is trying to address these concerns so that pharmacies can get larger supplies and provide the medications to patients who are coming in with valid prescriptions.

Connolly said that the White House has put in place several programs to help end the opioid epidemic, including creating more drug-free community coalitions, increasing access to opioid reversal agents, and expanding access to buprenorphine and methadone. ■

Get ready: COVID-19 therapeutics transition to the commercial market

Clarissa Chan, PharmD

As pandemic uncertainty dissipates, COVID-19 therapeutics are transitioning from U.S. government–procured sources to the commercial market. Health care providers—and especially patients—will encounter changes in distribution, access, and affordability for COVID-19 medications such as Paxlovid and Lagevrio.

What problems may arise with the transition of COVID-19 therapeutics to the commercial market?

Transitioning to payment through a typical insurance model has its challenges for both pharmacists and patients.

"For pharmacists, [medications] may require prior authorization, such as confirmation of a positive COVID-19 test [result], which may be the same as now," said Robert Popovian, founder of Conquest Advisors and chief science policy officer at Global Healthy Living Foundation. He said he thinks it's unlikely PBMs will make it difficult either, considering it's an infectious disease with significant mortality and morbidity consequences.

With the impacts on distribution, Popovian said patients may face an out-of-pocket cost requirement based on their benefit design.

How can pharmacists inform patients and other health care providers of the changes?

"Pharmacists can guide patients to use the enhanced COVID-19 medications locator created by HHS (www.treatments.hhs.gov) to find COVID-19 test-to-treat locations and locations that are participating in patient assistance programs," said Morgan Howard, PharmD, senior manager of practice implementation at APhA.

There may be locations that offer outpatient COVID-19 medications and are not listed on this website. The locations displayed on this locator have reported availability of Paxlovid, Lagevrio, or Veklury within the last 60 days, she said.

Where should pharmacists look for the most recently updated information on commercial distribution?

Pharmacists should refer to reliable sources, such as official government health agencies, pharmaceutical companies, and professional organizations, for the most updated information on commercial distribution of Paxlovid and Lagevrio, said Howard.

"These sources can provide guidance on distribution timelines, allocation strategies, and availability in different regions," said Howard. "The Administration for Strategic Preparedness & Response (ASPR) has created guides intended to provide direction as the U.S. government prepares to wind down the current distribution of government–procured COVID-19 therapeutics and transitions the COVID-19 oral antiviral treatments to the commercial market."

Associations such as APhA and the National Alliance of State Pharmacy Associations have been directly engaged with ASPR in finding solutions by disseminating resources that provide guidance on distribution timelines, allocation strategies, and availability in different regions, Howard said.

Will Paxlovid and Lagevrio be affordable for patients?

Efforts are underway to ensure that Paxlovid and Lagevrio remain affordable for patients, particularly those facing financial barriers to accessing treatment.

This may include reimbursement programs for those who are uninsured or insured by Medicare and Medicaid, and patient assistance programs aimed at reducing out-of-pocket costs and improving affordability. These programs include Pfizer's PAXCESS program and Merck Programs to Help Those in Need (merckhelps.com), said Howard.

How is FDA monitoring the safety and efficacy of Paxlovid and Lagevrio?

As part of the emergency use authorizations for Paxlovid and Lagevrio, FDA requires that both health care providers who prescribe the product and sponsors for each product report to FDA all serious adverse events and medication errors considered to be potentially related to the product.

Once FDA approves a product, health care providers are encouraged to report adverse events to either the drug company or FDA via the MedWatch program, said Charles Kohler, an FDA spokesperson.

FDA's principal repository for drug safety information is the FDA Adverse Event Reporting System (FAERS) database, which contains adverse event reports, medication error reports, and product quality complaints resulting in adverse events that were submitted to FDA.

The database is designed to support FDA's postmarketing safety surveillance program for drug and therapeutic biological products. It has also been used to conduct surveillance for all COVID-19 emergency use authorization products, Kohler said.

If a potential safety concern is identified, further evaluation using other data sources can be performed and may result in regulatory action such as updating a product's labeling information, restricting the use of a drug, communicating new safety information to the public, or in rare cases removing the drug from market, according to Kohler. ■

Review the latest information on the sunsetting of the U.S. government's COVID-19 Therapeutics Distribution Program: https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/COVID19-Tx-Transition-Guide.aspx ■

ON THE COVER

Health care teams for gender-affirming care have a clear place for pharmacists

Loren Bonner

Hormone therapy, specifically estradiol and testosterone, are familiar drugs. Pharmacists know how they interact with other medications. What is less clear is how pharmacists fit into the changing landscape of clinics and health care teams as transgender individuals seek gender-affirming hormone therapy, a medical intervention to align appearance with gender identity.

"Gender-affirming hormone therapy dates back decades, but is a domain more providers are going to need to familiarize themselves with as it escalates in practice," said Elisa Stanger, PharmD, a primary care clinical pharmacist from Cleveland Clinic's Department of Pharmacy.

Stanger led a research study that showed exactly how clinical pharmacists could fit into the workflow of gender-affirming care for gender diverse patients in a community ambulatory setting.

At Cleveland Clinic's Center for LGBTQ+ Care, the medical director and the institution's primary care pharmacists worked to update their CPA to include gender-affirming hormone therapy when patients come in for routine gender-affirming hormone therapy follow-up.

The study, published in the January/February 2024 issue of *JAPhA*, details the protocol the clinic used when a pharmacist managed gender-affirming hormone therapy for stable patients after they completed hormone titration provided by a physician or an advanced practice provider. In Ohio, pharmacists practicing under a CPA with a physician or other health care provider are allowed to order laboratory tests for patients and then modify drug therapy on the basis of those test results.

"We've seen published literature with pharmacists on these types of care teams," said Stanger. "We feel we are showing where pharmacists can exactly fit into the workflow through a concrete protocol."

In the updated CPA at Cleveland Clinic's Center for LGBTQ+ Care, pharmacists can perform services to manage transgender care and gender transition as a primary diagnosis. Comorbid conditions that were elected to be included within the CPA update were hyperlipidemia/statin management, diabetes, smoking cessation, and hypertension.

"These comorbid conditions were specifically chosen given that they can develop or worsen with long-term hormone therapy and are imperative to monitor and treat accordingly," wrote researchers.

At the clinic, pharmacists only see patients already established on gender-affirming hormone therapy for at least 6 months, at least 1 year after transition, and with a primary care provider managing their gender-affirming hormone therapy.

In the CPA, pharmacists can manage both feminizing (i.e., estrogens, antiandrogens, and progesterone) and masculinizing (i.e., testosterone and α-alpha reductase inhibitors) hormone therapy.

Testosterone levels were included for masculinizing hormone surveillance. Similarly, estradiol levels and testosterone levels were included for feminizing hormone surveillance if there were any concerns about hormone efficacy.

assess serum potassium levels with the use of spironolactone; hematocrit and the risk of polycythemia with masculinizing hormone therapy; and prolactin and the risk of hyperprolactinemia for those taking estrogen therapy.

"Our practice settings enable us to address a case that is as thought-provoking as it is interesting, allowing us to uncover real-world implications of pharmacist-led initiatives across different states and health systems."

Given that elevations in liver enzymes can occur with testosterone, estrogen, and cyproterone acetate, pharmacists at the clinic are able to order a complete metabolic lab panel for patients. They also monitor and

Given the increased risk of hyperlipidemia and diabetes with hormone use, clinical Cleveland Clinic pharmacists are able to order a lipid panel and A1C test. Stanger noted that the protocol is still fairly new at the clinic.

Table 1. Services provided by clinical pharmacists at each clinic

Service provided	California clinic	Mississippi clinic	Florida clinic
Hormone therapy	✔	✔	✔
PrEP/PEP counseling	✔	✔	✔
Immunizations	✔	✔	✔
Smoking cessation	✔	X	X
Physical assessments	✔[a]	X	✔[b]
Laboratory test ordering	✔	✔	✔

[a]Advance practice; [b]Collaborative drug therapy management.
Reproduced with permission from Phan et al. doi.org/10.1093/ajhp/zxad328.

Gender-affirming hormone therapy management was only approved to be added to the pharmacists' CPA in May 2022. Pharmacists started seeing patients at Cleveland Clinic's Center for LGBTQ+ Care in February 2023.

"This is only a brief report, there is more to come," she said.

State level

Of course, a pharmacist's ability to do any of this hinges on their state of practice—not only the state's pharmacy scope of practice law, but also any laws pertaining to gender-affirming care, which can vary by state.

A report published on December 29, 2023, in the *American Journal of Health-System Pharmacy* explored how pharmacist-led services are integrated into practice in three states with varying legislation for sexual and gender minority populations.

Researchers looked at services in California, Mississippi, and Florida, specifically, in order to get a comprehensive view of the challenges—and opportunities—for putting pharmacist-led services into practice. These three states have different legislative and professional scopes for clinical pharmacists, and they are all culturally different as well.

"Our practice settings enable us to address a case that is as thought-provoking as it is interesting, allowing us to uncover real-world implications of pharmacist-led initiatives across different states and health systems," said lead author of the study Tam Phan, PharmD, from the University of Southern California.

The services provided by clinical pharmacists at various sites in these states included gender-affirming hormone therapy management; HIV antiretroviral medication adherence programming; primary care and chronic disease state management; and involvement in care related to mental health, psychiatry, and substance use as well as sexual health services.

In Florida, for instance, pharmacists work in a sexual and gender minority health clinic network that has been designated as a federally qualified

Table 2. Laboratory parameters for masculinizing and feminizing hormone surveillance

Follow-up time frame	Laboratory parameters for hormone surveillance	
	Masculinizing	Feminizing
Provider-led laboratory parameters		
Baseline laboratory tests (initial visit[a])	Hemoglobin A1C, CMP, lipid panel	
1-month follow-up	None	BMP (if spironolactone is used)
Every 3 months for the first 12 months	CMP, CBC, total T	CMP, E2, total T
Provider- or pharmacist-led laboratory parameters[b]		
Every 6 months CMP		
Clinician discretion	Hemoglobin A1C, lipid panel, CBC	
If there are symptoms of prolactinoma	N/A	Prolactin
If there are concerns about hormone efficacy	Total T, free T	Total T, E2

Abbreviations used: BMP, basic metabolic panel; CMP, composite metabolic panel; E2, estradiol; GAHT, gender-affirming hormone therapy; free T, free testosterone; total T, total testosterone.
[a] Initial visit defined as first appointment with the provider for the start of GAHT; [b] Starting approximately 1 year after transition initiation, after hormone titration is completed. Provider-led laboratory parameters are ordered and monitored by the physician or advanced practice provider managing GAHT. Pharmacist-led laboratory parameters are ordered and monitored by the consulted pharmacist.
Reproduced with permission from Stanger et al. doi: 10.1016/j.japh.2023.10.006.

health center look-alike. Through a collaboration with a local college of pharmacy, clinical pharmacy services were offered to providers at all three clinic locations. Through the collaboration, providers determined that pharmacists would benefit patients and providers most with services focused on polypharmacy and appropriate medication use.

Pharmacy practice in Florida allows for an advanced scope of practice through the scope of collaborative drug therapy management. Legislation is currently progressing through the Florida legislature to expand existing "test to treat" CPAs to include HIV PrEP.

At all three clinics in these respective states, the lead pharmacists have worked with administrators to develop CPAs to expand the scope of practice for medication management services.

Given that many medications prescribed in gender-affirming care are used off-label, all three sites drew on available evidence-based guidelines to inform clinical decision-making, including, but not limited to, the World Professional Association for Transgender Health Standard of Care (version 8), the Endocrine Society clinical practice guideline, and guidelines from the UCSF Center of Excellence for Transgender Patients.

Phan said that notwithstanding the diversity of practice settings, there was a striking similarity in the services rendered by pharmacists.

"This phenomenon likely arises from a shared recognition among the [pharmacists] of various health disparities prevalent across various disease states, such as gender-affirming hormone therapy and HIV [antiretroviral drugs] adherence," he said.

As the authors noted, putting these services into practice requires a thorough evaluation of legislative and regulatory barriers, the diversity of patients' sociodemographic characteristics, and the systemwide scope of practice for pharmacists.

The report also focused on how pharmacist-led initiatives could enhance health outcomes and bridge health care gaps for sexual and gender minority populations.

"[Pharmacists] expertise proved essential in navigating intricate medication schedules, supporting adherence rates, and imparting knowledge

on correct medication usage," said Phan.

Sexual and gender minority populations also report negative experiences with health care providers, which keeps many away from seeking out health care in the first place.

Stanger said that some of their patients travel far distances to seek care at Cleveland Clinic's Center for LGBTQ+ Care.

"Patients will post on Reddit and other social media platforms if they find a good [gender-affirming hormone therapy] provider—we found they did that with our Cleveland Clinic providers," Stanger said.

Psychotropic medication interactions

Phan said their report also supports the need for pharmacists' involvement in mental health care due to the higher risk of mental health conditions among sexual and gender minority individuals.

Research has shown that transgender people are at a greater risk of mental health conditions such as depression, anxiety, suicidal ideation and suicide attempts, and substance use.

Among transgender individuals who have access to medical care, emerging data suggest a high prevalence of psychotropic medication use.

According to a study published in the January/February 2024 issue of *JAPhA*, among more than 300 transgender people on gender-affirming hormone therapy, including either estradiol or testosterone therapy, more than half had at least one order for a psychotropic medication. Of this cohort of individuals, more than one-third were on two or more psychotropic medications with overlapping treatment durations.

Research has shown that transgender people are at a greater risk of mental health conditions such as depression, anxiety, suicidal ideation and suicide attempts, and substance use.

For the authors of the study, it was clear that pharmacists can identify and address potential drug—hormone interactions between hormone therapy and psychotropic medications—and they wanted to demonstrate that.

"Because potential drug–hormone interactions exist between certain psychotropic medications and gender-affirming hormone therapies, pharmacists may play an important role in identifying and managing drug therapy problems, including drug–hormone interactions, for transgender people," said lead study author Lauren Cirrincione, PharmD, MPH, from the Department of Pharmacy at the University of Washington.

"Reassuringly, most types of psychotropic polypharmacy we observed in our analysis appeared to align with current mental health treatment guidelines," she said. "However, the number of people with at least one potential drug–hormone interaction between psychotropic medications and concurrent hormone therapy was significantly higher among those with psychotropic polypharmacy."

Cirrincione said their small hypothesis-generating analysis was designed to provide a better understanding of the patient-level psychotropic medication burden and potential drug therapy problems for transgender individuals on gender-affirming hormone therapy for future pharmacist-led interventions.

"Follow-up investigations, including prospective pharmacokinetic studies, are needed to characterize the potential drug–hormone interactions observed in this analysis," Cirrincione said.

She added that not every transgender person wants or has access to medical care or gender-affirming hormone therapy.

"Given our focus on potential interactions with hormone therapy, our analysis was limited to transgender people on gender-affirming hormone therapy within a single health system," she said. "Future investigations of psychotropic polypharmacy should consider characterizing the patient-level psychotropic medication burden for transgender people not on hormone therapy, and comparing the medication burden both before and during hormone therapy when possible."

At Cleveland Clinic's Center for LGBTQ+ Care, mental health conditions were not part of the CPA that could be managed directly by the pharmacist at the time of protocol development and therefore not included as comorbid conditions. The authors did, however, acknowledge how important mental health conditions are as they relate to gender-affirming care. ■

Pharmacists as champions in access to hormone therapy for transgender and gender-diverse individuals

Clarissa Chan, PharmD

"One of the most powerful ways pharmacists can help facilitate access to gender-affirming hormone therapy is by being an advocate for gender-affirming care," said Julianne Mercer, PharmD, pharmacotherapy resident at the University of Texas at Austin College of Pharmacy and University of Texas Health Science Center at San Antonio. WHO defines gender-affirming care as "a range of social, psychological, behavioral, and medical interventions designed to support and affirm an individual's gender identity."

Transgender and gender-diverse individuals face substantial health disparities, including an elevated susceptibility to self-harm, suicide, mental health challenges, and substance use compared to the general population.

Findings from a review published in the November/December 2023 issue of *JAPhA* can help pharmacists better understand gender-affirming hormone therapy (GAHT) and their related health concerns to help facilitate a patient's access to GAHT, with emphasis on patient treatment goals, preferences, and tolerability in therapy choices.

"With the increase in legislation isolating this group and the prevalence of reported negative experiences in health care and other stress-inducing factors, we can identify these as potential elements contributing to the minority stress theory," said Mercer, who was the lead author of the *JAPhA* review.

This theory suggests that negative social experiences such as isolation, stigma, and discrimination pose risks to a person's physical and mental health outcomes.

"Therefore, advocating for equitable care and environments of belonging is crucial, impacting direct social experiences as well as potentially physical and mental health outcomes as well," said Mercer.

Information to assess risks, benefits

Several of the links explored in the study—particularly in relation to CV and cancer risks—are inconclusive. They have not demonstrated much

difference from that of cisgender counterparts, and need to be investigated further.

"Health care providers should still inform their patients that the risks associated with [feminizing hormone therapy] and [masculinizing hormone therapy] are not completely understood; most of what we know has been derived from trials conducted on cisgender individuals," said Justina Lipscomb, PharmD, BCPS, clinical assistant professor at the University of Texas at Austin College of Pharmacy and University of Texas Health Science Center at San Antonio, University Health System, an author of the study.

The target ranges for serum estradiol and testosterone levels in transgender and gender-diverse patients taking GAHT are also based on reference ranges for sex hormones in cisgender patients.

However, dose adjustments should be made in accordance with each patient's needs, goals, and safety, she said.

Before starting therapy, patients should be informed of the potential GAHT impacts on fertility, said Lipscomb.

"The benefits of gender-affirming care are best achieved after patients have expressed their goals and been provided with information to assess the risks and benefits," she said. "Every patient should feel empowered to verbally express their needs and be permitted to seek the interventions, whether pharmacological or non-pharmacological, that affirm their gender identity."

Role of pharmacists

As with any treatment, health care providers have a duty to communicate the risks of therapies and any knowledge gaps in existing literature. For GAHT in particular, the data on renal dosing, CV health, fertility, and cancer-related health outcomes are evolving.

"Existing data present conflicting information," said Mercer. "Pharmacists should acknowledge that for many of these health risks, there are limited established causality explanations between appropriately managed GAHT and increased negative health outcomes."

However, there are still risks associated with GAHT, that vary across drug doses and formulations, that should be communicated to providers and patients to ensure their safety and awareness of potential adverse outcomes, said Mercer.

"The most encompassing communication strategy involves acknowledging current research limitations studying long-term outcomes in this population, communicating patterns, and trends based on available data, and leveraging clinical judgment to educate based on a patient's concomitant risk factors," said Mercer.

"The benefits of gender-affirming care are best achieved after patients have expressed their goals and been provided with information to assess the risks and benefits."

"A patient suffering from gender dysphoria may seek maximum hormonal therapy, while another patient may choose not to receive any hormone therapy," said Lipscomb.

Although hormone therapy offers many benefits to patients, pharmacists must be aware of potential adverse effects, she said.

"For example, in individuals with testes, prolonged estrogen exposure may result in testicular atrophy," said Lipscomb. "When estrogen therapy is discontinued, sperm production may not fully recover, reducing the possibility of conception."

Need for updated knowledge

While pharmacists are poised to offer guidance and education to patients and fellow health care providers concerning associated risks, many pharmacists feel ill-equipped to handle GAHT.

"It can be a challenge to locate comprehensive and accessible resources regarding GAHT post-pharmacy school," said Lipscomb. "However, first-line resources include standards of care documents and guidelines like those produced by World Professional Association for Transgender Health (WPATH), UCSF Transgender Care, and the Endocrine Society."

Podcasts and online videos covering topics on GAHT such as the ASHP Therapeutic Thursdays and the NIH virtual meeting on health disparities among sexual and gender minorities are also valuable resources, said Mercer.

Another strategy is to proactively create learning opportunities. "For instance, in a community pharmacy, a pharmacy leader could introduce readily available guides that provide resources for promoting inclusive care [such as Human Rights Campaign and APhA]," said Mercer.

Updated reviews of knowledge and strategies can empower pharmacists to deliver compassionate and well-informed patient care for individuals undergoing GAHT. ■

Study shows significant drop in prescription naloxone pricing

Elizabeth Briand

More than 112,000 Americans died as a result of opioid overdoses in 2023, a sobering reminder that the opioid crisis is far from over. Naloxone has proven to be a powerful tool in the ongoing effort to save lives, but its cost has been prohibitive for some. Fortunately, a recent study has shown significant price reductions for prescribed naloxone, making it more affordable for individuals at risk of overdose.

The study, published in the January 29, 2024, issue of *JAMA*, shows that between 2018 and 2022, the number of dispensed naloxone prescriptions increased 187.42%. At the same time, the out-of-pocket cost per prescription decreased 55.5% from $22.51 to $10.02.

Confluence of factors

A number of factors may have contributed to this decrease. "We think that price negotiations, market competition, and shifts in pharmacy benefit designs for insurance-paid prescriptions may have lowered [out-of-pocket] costs," said Xinyi Jiang, PhD, from CDC's Division of Overdose Prevention and lead author of the study. "For example, the approval of the first generic naloxone nasal spray by FDA in April 2019, equivalent to Narcan with lower costs, may have played a role in decreasing the overall out-of-pocket costs for naloxone."

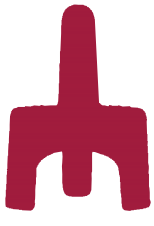
Coprescribing requirements may also be shifting out-of-pocket costs.

The federal government has been actively working to increase the availability of naloxone as well, such as allocating funding for the State Opioid Response Grant Program, which included funds to enhance naloxone distribution. This, too, could have contributed to price decreases, said Jiang.

OTC naloxone

Today, naloxone is available over the counter to anyone who wants or needs it. Sooner rather than later, that availability may also contribute to improved affordability.

"It is exciting to see FDA's approval of over-the-counter naloxone," said Jiang. "The availability of OTC naloxone means more individuals can access it not only in drug stores without prescriptions, but also in supermarkets, convenience stores, gas stations, and vending machines."



"We are in a public health emergency for opioid overdose and all recognized barriers to naloxone can and should be lifted."

Federal and state governments as well as advocacy organizations and the media may also have influenced pricing, said Jeffrey Bratberg, PharmD, clinical professor at the University of Rhode Island's College of Pharmacy. "More insurers are covering more products due to statutory requirements like in Rhode Island."

The suggested retail price for OTC naloxone is $44.99. "This price is lower than the out-of-pocket costs for those without insurance, but higher than the out-of-pocket cost for insurance-paid prescriptions, based on our study," said Jiang. "It is important to note that while OTC naloxone enhances accessibility, some families facing financial challenges may still find it difficult to afford." With that in mind, she added, "ongoing public health efforts such as community naloxone distribution and harm reduction programs, which provide free naloxone, should be continuously implemented."

Work still to be done

One group of Americans who did not see lower out-of-pocket costs were older adults. "What we found was that individuals aged 65 years or older had a higher out-of-pocket cost compared to those aged 18 to 64 years," said Jiang.

Specifically, the mean cost was more than $10 higher. The primary driver in that disparity appeared to be attributed to Medicare.

"People over 65 are increasingly larger segments of the overall proportion of overdose deaths, along with increases among teenagers and BIPOC [Black, indigenous, and other people of color] communities," said Bratberg. "All Medicare prescription plans and essentially all insurers should cover all evidence-based naloxone forms at zero out-of-pocket costs. We are in a public health emergency for opioid overdose and all recognized barriers to naloxone can and should be lifted."

Pharmacists can provide an invaluable lifeline in helping individuals access naloxone. "If individuals find it challenging to afford naloxone, pharmacists can provide resources for accessing [it for free]," said Jiang. "Different states have varying resources and programs. Pharmacists are encouraged to be familiar with local free naloxone resources and share this information with individuals who may need it."

Bratberg encouraged pharmacists to be even more forthright in their provision of naloxone. "We need pharmacies to boldly and robustly provide OTC naloxone along with other harm reduction options like syringe disposal, fentanyl test strips, and wound care, as a harm reduction package," he said. "This not only helps with people finding these products in one spot, but also destigmatizes harm reduction more generally." ■

Pharmacies expand access to hormonal contraceptives

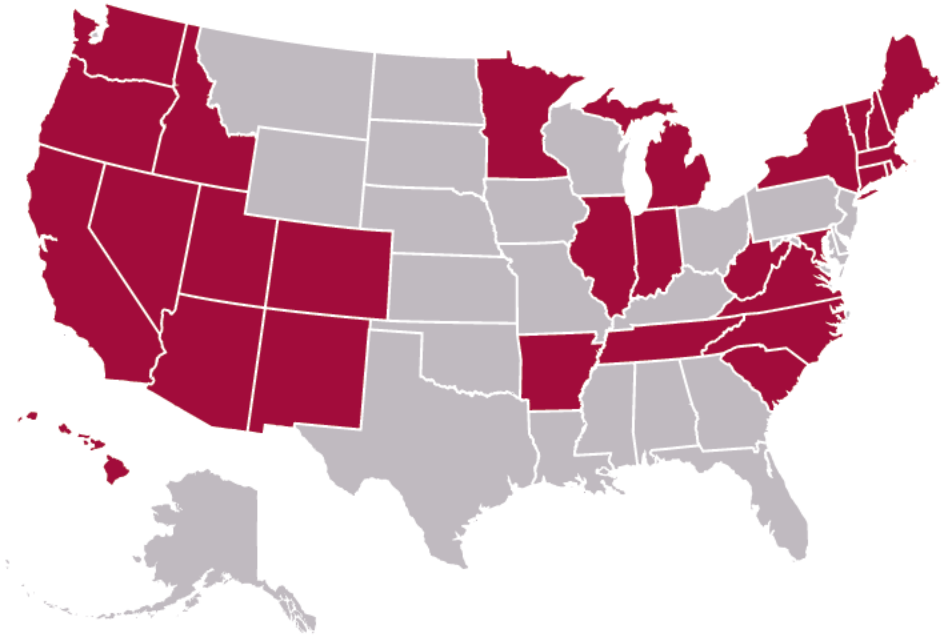
Olivia C. Welter, PharmD

For nearly a decade, pharmacists in select jurisdictions have been able to prescribe hormonal contraceptives, and nearly every year, more states pass legislation granting pharmacists this authority.

A June 2023 survey published in the *Journal of Women's Health* found that roughly 71% of women aged 18 to 44 years said they were interested in pharmacy-based contraception.

But there's a lot for pharmacists to keep up with in this arena. Recent developments, including an OTC birth control pill, have started shaking up the world of contraceptives.

How can pharmacists best put birth control services into practice in today's world?



Adapted from www.cnn.com/2024/01/12/health/otc-birth-control-pharmacist-prescribed

Currently, 29 states allow pharmacists to prescribe hormonal contraceptives.

Birth control goes OTC

In July 2023, FDA approved Opill (norgestrel 0.075 mg), the nation's first hormonal contraceptive available over the counter. Opill's manufacturer, Perrigo, annouced its first shipments of Opill to pharmacies and retailers nationwide in March 2024. A one-month supply is estimated to cost $20, while a 3-month supply is estimated at $50. Pharmacies will be able to set their own price for Opill when it hits pharmacy shelves.

Opill is a progestin-only birth control pill, meaning it doesn't have an estrogen component like many prescription contraceptives. Sometimes referred to as minipills, progestin-only pills require more diligence than combination pills. According to Mayo Clinic, if the patient skips a pill or takes one more than 3 hours later than their scheduled time, a backup form of contraception must be used for at least 2 days.

Although Opill will be available over the counter for anyone who would like to purchase it, pharmacists should plan to offer counseling to ensure patients are aware of the need for a consistent routine in taking the medication. Progestin-only pills are good options for individuals who have high BP, are overweight, are 35 years or older, smoke tobacco, or have a history of blood clots or breast cancer.

Another manufacturer, Cadence, is currently working to gain FDA-approval of an OTC combination pill called Zena (ethinyl estradiol 0.02 mg and levonorgestrel 0.1 mg). If approved, Zena would be the first birth control pill containing an estrogen component available without a prescription. This would further increase access for individuals who prefer to take a combination pill rather than a progestin-only pill.

Pharmacists as prescribers

Currently, 29 states allow pharmacists to prescribe hormonal contraceptives. To make an informed decision, pharmacists will usually need to take a patient's BP, discuss the patient's goals for birth control, and conduct a full medical history to evaluate for any contraindications if the patient is receiving estrogen-containing pills. Because many states don't allow phar-

macists to bill for their time performing these patient care services when a prescription is given, the cost is typically passed on to the patient.

It remains to be seen whether insurance will cover Opill. Most insurance policies typically won't cover OTC products, which means patients would need to pay cash for Opill. If they have a prescription, the pharmacy is able to bill insurance. On the other hand, if a patient gets that prescription from a pharmacist, the pharmacy may charge a service fee—typically anything from $30 to $50 to the patient. Does the patient want to pay the OTC price or pay for a consultation to get a prescription? Either way there will likely be an out-of-pocket cost associated.

In other cases, due to lack of reimbursement for services, many pharmacies opt out of providing birth control services even if their state allows it. One example is Tennessee. Although legislation passed allowing pharmacists to prescribe birth control under a collaborative practice agreement, the law states that pharmacies may not require patients to pay an administrative fee for the service if they use insurance to cover their prescription. Most patients opt to use their insurance if they have it, which means the pharmacy will only get paid for the cost of the medication and not the time spent performing the consultation.

It remains to be seen whether insurance will cover Opill.

Pharmacy resources

Despite these hurdles, many pharmacists still choose to offer patients birth control services and there are several strategies pharmacies can consider for putting these services into place.

According to a study published in the January/February 2024 issue of *JAPhA*, researchers found that most of the interviewed pharmacists in San Francisco said they were successful in implementing birth control services when they established company protocols, had advertising strategies, and employed pharmacists who were interested in furnishing birth control services to increase patient access. Some specific advertising strategies listed by pharmacists were banners in the pharmacy, advertisement on their website, and flyers at the pickup window. Pharmacists also noted that demonstrating ease of access to patients was an effective method for demonstrating the value of the service to patients.

For pharmacists looking for direct resources, the Birth Control Pharmacist website houses resources to help pharmacies feel prepared to offer a new birth control consultation program.

Pharmacists should also consult their state's Board of Pharmacy rules to ensure they are following all regulations required for prescribing birth control. State pharmacy associations are also knowledgeable about state-level regulations and can share more information with pharmacy professionals who are interested in learning more about implementing a birth control prescribing service in their practice. ■

Shaping the future of hormonal contraceptive care

On February 28, 2024, APhA and the Contraceptive Access Initiative (CAI) concluded the Accessible Consumer Choices: Shaping the Future of Contraceptive Care at Pharmacies Summit. The summit convened a diverse range of private and public sector partners, including representatives from the White House Gender Policy Council, HHS, pharmacy businesses, pharmacists, patient advocates, and other influential voices. Throughout the day, participants engaged in fruitful discussions, collaborative sessions, and strategic planning aimed at advancing accessible and equitable hormonal contraceptive care at pharmacies.

"By addressing barriers and fostering collaboration, we are making significant strides in ensuring patients have broader access to essential health care services provided by pharmacists," said Michael D. Hogue, PharmD, FAPhA, FNAP, FFIP, APhA's executive vice president and CEO.

Participants identified federal and state policy barriers and implementation obstacles that currently limit patient access to pharmacist-provided hormonal contraceptives and worked together to develop recommendations aimed at overcoming policy and implementation barriers, ultimately increasing access to pharmacist-provided hormonal contraceptives.

Partnerships between the public and private sectors as well as between patient advocacy groups and the pharmacy community were fostered to collectively address and overcome existing barriers and ways in which to increase public awareness regarding pharmacist-provided hormonal contraceptives as a viable and accessible option to meet reproductive health care needs were discussed.

"Through our partnership with APhA on this convening and with the thoughtful expertise of every participant, we have identified significant areas of common interest," said Dana Singiser, partner at Keefe Singiser Partners and CAI cofounder. "We look forward to continuing our work toward making contraception truly available and accessible to all."

The summit's outcomes and recommendations will be compiled into a comprehensive report, which will be made available to the public and policymakers. ■

Pharmacists stuck between legal rock and contractual hard place

Sonya Collins

Pharmacies are struggling—both the independents and the chains. The ACT Pharmacy Collaborative, a partnership with CPESN and pharmacy academia, reported closures of 244 pharmacies including independents and chains in 48 states in just the first 6 weeks of 2024. Add that to markedly slower postpandemic sales and a diminished workforce, already meager reimbursements, and hefty DIR fees from PBMs making increasingly deeper cuts into pharmacy profits and rendering numerous businesses unsustainable.

Pharmacists have little recourse to protect themselves. Many states prohibit pharmacists from refusing to fill a prescription based on the reimbursement rate, while contracts with PBMs may include gag orders that keep pharmacists from telling patients they are taking a hit by filling the prescription.

"Technically, we can be penalized for having conversations with our patients about it," says Jade Ranger, PharmD, co-owner of The Prescription Shoppe in Williamsburg, VA. "Not only are you not supposed to refuse to fill prescriptions based on the reimbursement, but you're also not supposed to tell them that."

This "rock and a hard place" scenario is having far-reaching effects on the community pharmacy landscape and the patients served by it.

Not just the little guys

Combined, Rite Aid (which filed for bankruptcy in October 2023), Walgreens, and CVS shuttered 1,500 stores in the past 2 years, according to *The Washington Post*.

These closures sometimes send patients to nearby independent pharmacies. But crippling reimbursement rates threaten to keep independent pharmacies from obtaining the staff and resources they need to absorb new patients from the chain pharmacies.

According to a National Community Pharmacists Association survey, which aimed to gauge whether chain closures were an opportunity or a threat to independents, many independent pharmacists cited low reimbursement from PBMs as their top concern and a major barrier to absorbing patients displaced by closed chains.

Regardless, chain closures don't always result in new clientele for independent pharmacies. Patients at closing stores are often simply forced by their health plans to travel to another of the chain's locations to get their prescriptions filled or to use mail order.

Expanding pharmacy deserts

Many patients relegated to mail-order pharmacies can't travel the few extra miles to the chain's next-nearest location.

"In Philadelphia, some of these Rite Aids are closing in areas where there's no other pharmacy for miles," said Mayank Amin, PharmD, owner of independent Skippack Pharmacy in Skippack, PA. "A lot of people who live there are lower income and don't have a vehicle."

One in 10 U.S. residents lives more than 5 miles from a brick-and-mortar pharmacy. A 2021 analysis by the Rural Policy Research Institute found that 138 U.S. counties did not have a pharmacy. In the analysis, the counties least likely to have a pharmacy were inhabited by the most vulnerable patients. Evidence suggests that outcomes, including medication adherence, are better for patients who live near a pharmacy. Not to mention, Amin added, the critical role pharmacies showed they could play in a pandemic or a flu surge.

"Let's say, 10 years down the road, there are no brick-and-mortar pharmacies, is mail order going to have vaccine clinics or point-of-care testing to serve thousands of people?" he said.

Just to stay afloat

The Prescription Shoppe, which Ranger and her husband own and operate, lost $10,000 filling prescriptions in January. Since they cannot voluntarily refuse to fill, some pharmacists are choosing not to stock the drugs that lose money.

"We have to be careful of what we fill and don't fill," Amin said. "I have friends that fill 500 to 700 prescriptions a day, but they're operating at a loss by filling that many."

While contractually Amin cannot tell patients when he's taking a loss, he does ask if they'd be willing to let him transfer that particular prescription to a chain pharmacy or mail order.

In social media posts, he writes, "if you use an independent pharmacy and they tell you they can't get a specific brand-name drug from their wholesaler, read between the lines. They likely can't fill it because they are getting reimbursed from your insurance company lower than the cost that they buy the drug for."

Pharmacies are also turning to alternative revenue streams. Ranger and her husband recently opened a compounding pharmacy that works directly with long-term care facilities. They also administer self-injectables to squeamish patients for $5. They charge $20 for point-of-care flu and strep tests.

While cash revenue streams may keep individual pharmacies alive, they won't save the industry. Both Ranger and Amin stress the importance of political advocacy and joining forces with pharmacy associations to push for legislative changes that can save community pharmacies.

"I don't think change can happen unless it's done through advocacy," Amin said. ■

A system failure leads to late medication delivery and patient death

David B. Brushwood, BSPharm, JD

Hospitals can be held liable for causing harm to patients either due to the negligence of employed health care professionals (indirect liability) or for institutional negligence (direct liability). In a recent case from Illinois, a jury awarded $42.4 million against a hospital for institutional negligence.

Factual background

A patient was taken to the defendant hospital's emergency department on a Friday because his intrathecal baclofen pump required surgical replacement. The pump had stopped functioning correctly and the patient was experiencing baclofen withdrawal. The patient's physician "told the emergency physician about the concentration of baclofen that [the patient] required, which was 2000mcg." The physician "faxed a document to the emergency department that provided information about the required 2000mcg concentration of baclofen."

At 9:00 am on the following Monday, the patient's surgery was scheduled for 1:00 pm. The surgeon wrote in the patient care record, "Obtain baclofen kit from pharmacy!!!!!!!!!!!" He stated that the 11 exclamation points meant "that's an important step."

The director of pharmacy testified that it was not until 1:00 pm that the pharmacy received the order for intrathecal baclofen and that the nurse who communicated the order did not know the concentration that was needed. At 1:27 pm, the pharmacy was informed that the 2,000 mcg concentration was needed, but the pharmacy stocked only the 500 mcg concentration. The director located the 2,000 mcg concentration at another hospital and arranged for a courier service to obtain it, but the courier did not arrive with the baclofen until 5:00 pm.

The patient coded at 3:10 pm and was stabilized, but he did not regain consciousness. "It was undisputed that this event was the result of intrathecal baclofen withdrawal."

Successful surgery was performed at around 5:30 pm and lasted 30 to 40 minutes. The patient was placed on life support, and he died 2 weeks later.

The patient's estate sued the hospital, alleging that the hospital "allowed a system failure to exist, resulting in the delay of [the patient] receiving his intrathecal baclofen, and/or failed to ensure effective communication among [the patient's] healthcare providers."

The hospital appealed the jury verdict for the plaintiff, arguing that the institutional negligence claims "were not true claims of direct corporate negligence, but were predicated on the conduct of medical professionals exercising their medical judgment."

The director of pharmacy testified that it was not until 1:00 pm that the pharmacy received the order for intrathecal baclofen and that the nurse who communicated the order did not know the concentration that was needed.

Rationale

The appellate court first explained that under a theory of institutional negligence, "the law recognizes a duty on the part of hospitals to review and supervise the treatment of their patients, and this duty is administrative or managerial in character."

The court quoted testimony from an expert witness who explained that "a hospital is a system, meaning a complex series of activities and steps," and that a system failure occurs "when many things go wrong despite the safeguards built in, resulting in a bad outcome."

The court reviewed the evidence and concluded that "the plaintiff appropriately employed the theory of institutional negligence to impose direct liability on the part of the hospital." The court explained, "the facts of this case demonstrated that it was the responsibility of the hospital as an institution to procure the equipment and medication needed by a surgeon in the course of a particular surgery."

The jury verdict against the hospital was affirmed.

Takeaways

Hospital pharmacies cannot be expected to immediately supply all formulations of all medications in all concentrations at all times. Communication to the pharmacy department is necessary to allow for the timely acquisition of needed medications.

Effective communication systems can facilitate interdepartmental messaging. For example, a systematic communication avenue is necessary when the emergency department learns on Friday that the pharmacy department will need to supply an infrequently used medication to the surgery department on Monday.

Notations in electronic records indicating the need for specific medications should be immediately routed to the pharmacy department so that a sufficient supply of medication can be obtained to meet patient care needs. ■

Inpatient*Insights*

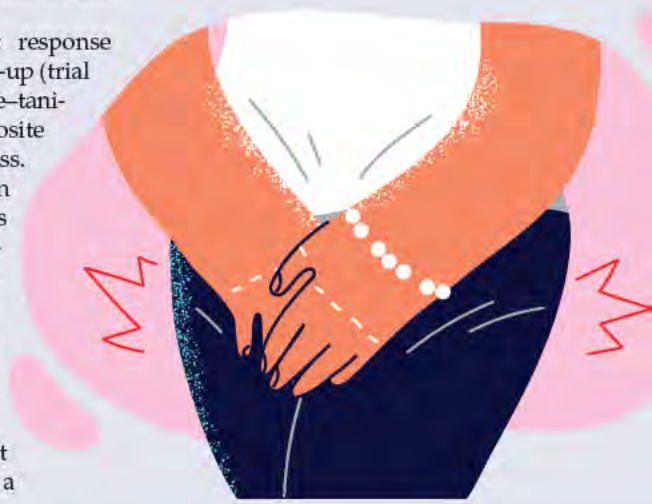
Cefepime–taniborbactam promising for treating complicated UTI

Widespread and emerging resistance to β-lactam antibiotics complicates management of serious UTI, which is responsible for at least 600,000 annual hospital admissions in the United States. Members of the CERTAIN-1 Study Team conducted a phase 3, double-blind, randomized trial to compare the efficacy of cefepime–taniborbactam, an investigational β-lactam and β-lactamase inhibitor combination, with standard treatment for complicated UTI. The study was published in the February 15, 2024, issue of *NEJM*.

The researchers assigned hospitalized adults with complicated UTI, including acute pyelonephritis, in a 2:1 ratio to receive I.V. cefepime–taniborbactam (2.5 g) or meropenem (1 g) every 8 hours for 7 days. Of the 436 patients who had a qualifying gram-negative pathogen against which both study drugs were active, 57.8% had complicated UTI, 42.2% had acute pyelonephritis, and 13.1% had bacteremia. Composite (microbiologic and clinical) success occurred in 70.6% of the patients in the cefepime–taniborbactam group and in 58.0% in the meropenem group.

Differences in treatment response were sustained at late follow-up (trial days 28–35), when cefepime–taniborbactam had higher composite success and clinical success. Adverse events occurred in 35.5% and 29.0% of patients in the cefepime–taniborbactam group and the meropenem group, respectively, with headache, diarrhea, constipation, hypertension, and nausea among the most frequently reported.

The authors concluded that cefepime–taniborbactam is a potential treatment option for patients with complicated UTI and acute pyelonephritis caused by Enterobacterales species and *P. aeruginosa*, including antimicrobial-resistant strains. ■



Continuation of temporary PPI treatment in ICU patients could result in harmful adverse effects

PPIs are commonly prescribed for critically ill patients, primarily for preventing stress ulcers. However, their use is not always terminated after the patient has recovered, leading to potential adverse effects from continued PPI use. Although mainly applied temporarily for stress ulcer prophylaxis, their application is frequently continued. In a study published in the February 2024 issue of *Critical Care Medicine*, researchers at the Ruhr University Bochum tested the hypotheses that nonindicated PPI therapy continued beyond hospital discharge is associated with increased morbidity, rehospitalization rate, and mortality.

The authors conducted a nationwide retrospective cohort study of over 11,000 ICU patients who received PPI therapy for the first time during an ICU stay without having an indication for its continuation between January 2017 and December 2018 with a 2-year follow-up. The cohort was stratified into two groups: patients without further PPI therapy and patients with continuation of PPI therapy beyond 8 weeks after hospital discharge. Study results showed that 42% of the patients continued PPI therapy without an identifiable indication, and that these patients had a 27% greater risk of pneumonia, a 17% greater risk of CV events, a 34% greater risk of rehospitalization, and a nearly 20% greater 2-year mortality risk.

These data, said the authors, demonstrate that unnecessary continuation of PPI therapy after hospital discharge may significantly impact morbidity and mortality. They recommend that health care providers ensure timely cessation of temporarily indicated PPI therapy. ■

Training improves pharmacist code response team

Pharmacist participation as members of the code response team in hospitals and emergency departments is associated with improved outcomes, including increased compliance with Advanced Cardiac Life Support algorithms and a decrease in medication errors and mortality. Despite this, most institutions lack formalized pharmacist training for code team responses. Researchers at Brigham and Women's Hospital in Boston evaluated the impact of a didactic and simulation-based code response training for pharmacists on self-perceived improvement and preparedness when responding to in-hospital medical emergencies. The study was published on February 22, 2024, in *JAPhA*.

An emergency response curriculum, facilitated by four lead clinical pharmacy specialists, was developed for staff pharmacists and pharmacy residents, and included a 60-minute didactic code competency lecture followed by two medical emergency simulations and a debrief after each scenario. Almost 75 pharmacists completed the training and 60 completed a post-course survey. Of those who completed the post-course survey, 70% were pharmacy residents. Of the participants, 95% believed the training should be required annually or multiple times a year and 100% of respondents felt the training was beneficial.

The authors concluded that the didactic and simulation-based learning improved the confidence and preparedness of pharmacists when participating as members of the hospital code team. They suggested that future studies should continue to evaluate pharmacist training and curriculum development in code team responses. ■

Stop or continue buprenorphine for chronic pain in the acute care setting?

Buprenorphine is used to treat acute and chronic pain as well as OUD. However, due to poor quality evidence supporting previous treatment guidelines, clinicians are faced with a challenge in how to manage emergency department (ED) and postsurgical patients who are already receiving buprenorphine for chronic pain. Discontinuing buprenorphine could pose the risk of opioid-induced hyperalgesia while continuing or modifying buprenorphine doses poses a risk of inadequately managing acute pain. Researchers at the Durham VA Health Care System in North Carolina conducted a cohort review involving patients receiving long-term buprenorphine therapy who either underwent a surgical procedure or presented to an ED for acute pain between January 1, 2012, and January 1, 2022, to evaluate treatment strategies.

Chart reviews were conducted for 70 patients to characterize buprenorphine treatment strategies and the addition of new pain medications. Chart review revealed incidence of OUD relapse, hospital re-presentation for pain or OUD, fatal and non-fatal overdose, and all-cause mortality and suicidality. Of those included in the study, 85% presented to the ED while 16% underwent surgical procedures; 79% had an OUD diagnosis. The total daily dose of buprenorphine or buprenorphine/naloxone from index date to discharge was continued in 90%, increased in 2.9%, decreased in 1.4%, and discontinued in 5.7% of cases. At discharge, 46% were prescribed an additional pain medication. Within 90 days of discharge, 7.1% of patients re-presented for pain or OUD relapse, 16% experienced an OUD relapse, 1.4% experienced new-onset suicidality, and 1.4% experienced all-cause mortality. No fatal or non-fatal opioid overdoses were observed.

The researchers concluded that the most commonly observed practice of continuing buprenorphine doses in patients with acute or postsurgical pain was effective and safe. They note that although further data are necessary to fully elucidate these findings, the data from their study, published on February 16, 2024, in *JAPhA*, may suggest that clinicians can safely continue buprenorphine doses in the acute pain setting in patients receiving these medications for chronic pain. ■

Study reveals impact of acute care pharmacists' role in U.S.

Aiya Almogaber, PharmD

Pharmacists play a critical role within the broad spectrum of multidisciplinary teams in inpatient care environments. According to research findings published January 14, 2024, in the *Journal of the American College of Clinical Pharmacy*, pharmacists are applying their versatile skill sets to improve patient care within the complex landscape of adult medicine.

Inpatient health care in the United States is defined by comprehensive medical services delivered within a hospital or health care institution. These services can range from diagnostic tests, surgical procedures, and nursing care to therapeutic interventions and more.

"I wasn't surprised by how much the pharmacists can do," said lead author Jennifer Szwak, PharmD, who has practiced in adult medicine for over 10 years. "It was exciting to see how many different disease states adult medicine pharmacists impact. I think this speaks to the adaptability of adult medicine pharmacists and the variety of patients for whom we care."

"The key takeaway is the need for pharmacists to continue to advocate for bedside clinical positions."

In just a 1-week timeframe, 33 pharmacists provided 988.5 hours of direct patient care, according to the study findings. A total of 4,488 interventions that spanned a wide variety of activities were documented, with the optimization and initiation of therapy emerging as predominant themes. Other activities included interpretation of diagnostic data or lab values, responding to drug information inquiries, and recognizing inappropriate therapy. The therapeutic categories most affected included antimicrobials, cardiovascular medications, and antithrombotics.

Foundational research

Szwak said the aim of their research was to convey a clear picture to pharmacy and hospital administrators about what adult medicine pharmacists can add to patient care.

"We wanted to provide an idea of the clinical activities an adult medicine pharmacist can provide, which may help expand current practice, establish pharmacist-to-patient ratios, or justify new pharmacist positions," said Szwak.

According to Heather Wilson, PharmD, a critical care clinical pharmacist at Moses Cone Hospital in Greensboro, NC, the study findings could allow for foundational development for clinical positions.

"As a current practitioner, I feel that the current pharmacy gap of care is in adult medicine units," said Wilson. She said that up until now, there hasn't been much research to demonstrate the typical workflow for clinical pharmacists and their interventions in this area of practice.

Proactive role, proactive findings

The study was a prospective, multicenter endeavor that used a 65-item survey to explore the clinical activities of inpatient adult medicine pharmacists. The survey was designed to collect information related to practice site types, geographic regions, daily duties, therapeutic interventions, and evaluation of those interventions.

Nearly 90% of the documented interventions were accepted, with 82% initiated directly by pharmacists. Notably, 277 potential outcomes were classified as "serious" or "potentially lethal" without intervention, underscoring pharmacists' proactive role and impact on patient care.

"Pharmacists have expertise in all organ systems and pharmaceutical classes. The quantification of time per activity gives other health care professionals a glimpse into the typical day of a clinical pharmacist, beyond operational responsibilities," said Wilson.

Laying the groundwork

This study's analysis can serve as a benchmark and also lays the groundwork for future research efforts.

"The key takeaway is the need for pharmacists to continue to advocate for bedside clinical positions," said Wilson.

As health care continues to evolve, this call for advocacy becomes a cornerstone for advancing the role of pharmacists in optimizing patient outcomes.

"I hope clinical managers and [clinical] pharmacists are able to use [this] information to expand the services and activities provided by the adult medicine pharmacy team," Szwak said.

Overall, this study is a launching pad for a broader exploration of the multifaceted contributions of inpatient adult medicine pharmacists, including their varying levels of experience, specialty, and involvement in therapeutic areas.

"This study provides a starting point for future studies exploring more details about the interventions being made, their impact on readmissions or lengths of stay, patient safety, or clinical outcomes. I see this study as the forward that is followed by many stories of adult medicine pharmacists improving clinical care for patients across the country," Szwak said. ■

Experts issue changes in ARDS treatment recommendations

Ariel L. Clark

Since the COVID-19 pandemic, the world has seen the extent of harm caused by lung disease and infection. Acute respiratory distress syndrome (ARDS) is one that results in significant inflammation that reduces the lungs' ability to exchange oxygen for carbon dioxide and leaves patients at high risk for hypoxia, which can lead to severe impairment and death.

Patients with ARDS are at risk for severe complications, and according to Yale Medicine, up to 40% of patients do not recover from the condition. In a clinical practice guideline update published in the *American Journal of Respiratory and Critical Care Medicine* in January 2024, experts in ARDS treatment compiled and summarized their recommendations, including treatment updates and supportive care measures, to aid clinicians in treating their patients.

Systemic corticosteroids recommendations

Corticosteroids have been used successfully in the treatment of other respiratory conditions, including COVID-19 and community-acquired pneumonia, due to their ability to reduce inflammatory markers and inflammation in the lungs. In previous treatment guidelines, they were not mentioned. But in the current update, experts recommend using systemic corticosteroids in patients with ARDS, with certain caveats.

First, clinicians should use their best judgment when deciding the dosing regimen and duration of treatment, as that was not decided by the panel of experts. Second, treatment should be initiated within 2 weeks of symptom onset. Finally, clinicians should closely monitor for adverse effects, especially in those patients who are immunocompromised, are diagnosed with metabolic syndrome, or are at high risk for systemic infections, such as tuberculosis.

VV-ECMO recommendations

Experts included venovenous extracorporeal membrane oxygenation (VV-ECMO) as another treatment option in the update. VV-ECMO is an external gas exchange system that removes carbon dioxide and reoxygenates blood in an external chamber before returning blood to the patient.

Guideline authors recommend the use of VV-ECMO in patients with severe ARDS who have been unsuccessfully managed with other therapies and supportive measures.

In the current update, experts recommend using systemic corticosteroids in patients with ARDS, with certain caveats.

Compared to the other recommendations in this update, experts noted that ECMO can be cost- and resource-prohibitive for many patients and health systems, leading to its conditional recommendation and use only after other measures have been exhausted.

Neuromuscular blockade

Patients with lung injury have successfully been treated with neuromuscular blocking agents (NMBAs) in several randomized controlled clinical trials in recent years. Despite their exact mechanism remaining unknown, panelists agreed to include their use in this guideline update given the multitude of data supporting their use.

However, the recommendation to use NMBAs comes with "low certainty of evidence," as the literature reviewed included variable sedation strategies that were not directly comparable.

Overall, the pool of data showed that NMBAs reduced mortality and increased off-ventilator days, but clinicians should be wary unless patients are in early (<48 hours), severe ARDS and should balance the decision to administer NMBAs with the risk of ICU-acquired weakness. And for patients with late and severe ARDS, experts did not make a recommendation, stating that further research should be done on appropriate timing of initiation, dosing, and duration.

Ventilator settings

Intubated patients require intricate ventilator settings to minimize risk of further lung injury and to improve patient outcomes. The guideline update includes a recommendation from experts to use higher positive end-expiratory pressure (PEEP) versus lower PEEP in patients with moderate to severe ARDS, while no recommendation could be made for mild ARDS.

Along with higher PEEP, the panelists recommended against the use of lung recruitment maneuvers, or when intermittent increases in PEEP settings are used for roughly 60 seconds, because studies have shown the potential for harm with these techniques.

While the updated ARDS guideline represents a significant step forward in helping clinicians improve patient care, guideline authors acknowledged the ongoing need for further research to strengthen their recommendations. They emphasized the importance of collaboration among health care professionals in deciding the best treatment strategies for individual patients.

As clinicians continue to treat patients with ARDS, they should continue collaboration, further research, and commit to evidence-based practice to further refine ARDS management and treatment. ■

Pharmacists improve access to medications in neurology clinic

Sonya Collins

The last 10 to 15 years have seen approvals of many new specialty and biologic drugs for neurological conditions. Often, these medications work faster than older traditional immunosuppressing medications, but optimum outcomes depend on starting the right medication as soon as possible.

While time is of the essence, specialty medications can come with additional hurdles. Foremost, providers need to get approval from the patient's insurance. Research published online on January 19, 2024, in *JAPhA* finds that pharmacists embedded in a neurology clinic may help patients clear these hurdles faster and improve overall access to neurology treatment.

"This study can help support the use of clinical pharmacists in neurology clinics and also, potentially be a roadmap for other institutions that may want to continue to expand ambulatory care pharmacy services," said Bethany Anderson, PharmD, lead author on the study and a clinical pharmacist at Cleveland Clinic.

Pharmacists helped patients start treatment sooner

Researchers carried out a retrospective chart review of patients started on a first or alternative medication for a neuroimmunology or neuromuscular condition before (pre-group) and after (post-group) pharmacists were integrated into the clinic. The study compared access between the two groups to initially prescribed medications and alternative medications within 90 days of prescription. The researchers examined the charts of 101 patients in the pre-group and 101 patients in the post-group.

Just over 87% of patients in the post-group started the initially prescribed medication within 90 days of prescription—up from just over 72% in the pre-group. Ninety percent of patients in the post-group started either the initial or alternative medication within 90 days compared to a little over 73% in the pre-group.

Nearly 64% of patients in the post-group had additional pharmacist involvement, which could include prior authorization approval assistance, drug information support, and medication liaison interventions, with an average of 4.7 pharmacist interventions at each pharmacy-led encounter.

"There's a lot of coordination between staff doing the prior authorization and the provider who prescribed the drug, and that's where we come in—right in the middle."

Pharmacists overcome barriers

Many of the medications seen in the researchers' chart reviews require prior authorizations or come with other prerequisites that must be met before patients can start treatment.

In the clinic, pharmacists helped coordinate vaccinations and baseline labs required prior to initiating therapy. They assessed and addressed abnormal labs and drug–drug interactions. They ensured patients completed step therapy when required. Pharmacists counseled patients on what might ultimately become lifelong therapy, educated them on proper administration, and helped them weigh the pros and cons of the options available to them when applicable. They made sure physicians' orders were followed to get the treatment to the patient sooner.

"There's a lot of coordination between staff doing the prior authorization and the provider who prescribed the drug, and that's where we come in—right in the middle," said Melissa Snider, PharmD, coauthor of the study and associate director of ambulatory care in the department of pharmacy at The Ohio State University Wexner Medical Center.

Interventions by pharmacists that helped expedite initiation of therapy may in some cases be seen as critical to care or even lifesaving.

"Patients with a recent MS relapse are not protected against another relapse until they have started a disease-modifying therapy. Patients with neuromyelitis optica spectrum disorder (NMOSD) can relapse at any time, which may result in permanent disability like vision loss and paralysis," said Margaret Hansen, PharmD, a specialty practice pharmacist in neurology at the Ohio State University Wexner Medical Center.

But the benefits pharmacists can bring to ambulatory care clinics aren't limited to neurology, Anderson said.

"Pharmacists could be considered in other clinics, especially those with a lot of specialty medications and medications that require a lot of education and monitoring." ■

Pharmacist-led HF clinic optimizes therapy and improves outcomes

Corey Diamond, PharmD

Chiefly managed by pharmacotherapy, heart failure with reduced ejection fraction (HFrEF) includes pharmacists on the health care team playing an increasingly pivotal role in optimizing therapy for patients. Findings from a study published in the *Journal of the American College of Clinical Pharmacology* on January 24, 2024, found that pharmacist-led guideline-directed medical therapy for patients with HFrEF resulted in a higher degree of optimal HF therapy and improved echocardiographic parameters compared to baseline.

Medication optimization

Ladhar and colleagues conducted a pharmacist-led medication optimization study at an outpatient telehealth clinic at St. Paul's Hospital within the Providence Healthcare health system in Canada. Eligible patients were referred by cardiologists and underwent virtual/telephone encounters with a pharmacist to optimize guideline-direct medical therapy.

The clinic's guideline-directed medical therapy targeted optimization of four medications: angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers; beta-blockers; mineralocorticoid receptor antagonists; and sodium-glucose cotransporter-2 inhibitors.

These medications were then systematically optimized per the Canadian Cardiovascular Society HF guidelines. In addition to managing a patient's medications, pharmacists screened for comorbidities and collaborated with physicians on prescriptions. Referral criteria for the PHARM-HF clinic included HFrEF diagnosis, left ventricular ejection fraction (LVEF) of less than or equal to 40%, stability, need for guideline-directed medical therapy optimization, regular blood-work capability, virtual care suitability, and exclusion from multidisciplinary HF clinic care.

The typical patient progression included two to six encounters over 6 months, with appointments every 1 to 3 weeks. The clinic operated 1 day per week, with patients discharged to referring physicians upon achieving maximum-tolerated therapy.

Outcomes and results

The study, called PHARM-HF, was a retrospective, pre–post study that evaluated chart reviews of 81 patients from January 2021 to August 2022. The primary outcome was the modified optimal medical therapy (OMT) score, a validated scoring system that quantifies the optimization of a patient's HF medication. An OMT score of suboptimal, acceptable, and optimal fell in the ranges of 0 to 4, 5 to 7, and 8, respectively.

The researcher's secondary outcomes were the proportion of patients on all four targeted medications at any dose and the proportion of patients on all four medications at 100% target dose.

The study findings demonstrated a statistically significant increase in the median modified OMT score of 6 at baseline compared to 8 at discharge. The proportion of patients considered to be on optimal therapy increased from 7% to 73% compared to baseline. Moreover, there was a notable improvement in treatment adherence, with the percentage of patients adhering to all four medication classes rising from 35% to 77%. Additionally, the proportion of patients reaching the target doses for guideline-directed medical therapy increased from 2% to 16%.

In terms of clinical outcomes, researchers found a cumulative incidence of HF hospitalization or death of 5%. About 40% of patients in the study had an echocardiogram available at a 1-year follow-up that demonstrated a statistically significant improvement in median LVEF compared to baseline, from 30% to 38%. The authors did not see a statistically significant improvement in quality-of-life KCCQ-12 scores, although only 20% completed the questionnaire at baseline.

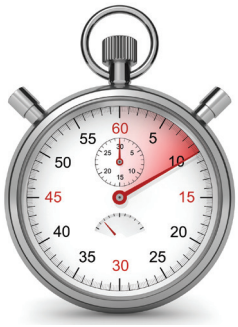
> Clinical pharmacists are beginning to play a crucial role in the optimization of guideline-directed medical therapy across the health care landscape.

Pharmacist's role

In the intricate landscape of CV health, the management of HFrEF is challenging for health care professionals. Guideline-directed medical therapy represents a comprehensive approach to treating HF, integrating evidence-based recommendations into a framework that aims to improve patient outcomes and enhance the quality of care—though adherence may not always be followed. As such, clinical pharmacists are beginning to play a crucial role in the optimization of guideline-directed medical therapy across the health care landscape.

The study highlighted that although many sites in Canada and the United States have successfully incorporated pharmacist-led HFrEF medication optimization services, this remains far from the standard of care, and resources are lacking in many HF clinics.

"As the global prevalence of HF continues to rise, the need for specialized clinicians in HF management is also increasing. Pharmacists' unique skills and knowledge of medications ideally position them to be involved in medication optimization," said the authors. ■



A minute with ...

Ellie Balken
Fourth-year student pharmacist at South Dakota State University
Member since 2018

"Membership in this organization has empowered me to grow personally and professionally, and my experiences have shaped the professional I aspire to be in the future. I am beyond grateful to APhA–ASP for the friendships and network of individuals who remind me daily what is so special about this profession. I am continually impressed by the leadership, intelligence, and kind hearts of pharmacists and student pharmacists and APhA has helped me establish a home within this incredible profession. "

How has APhA helped you establish meaningful connections?

Looking back on my freshman pre-pharmacy year, I had moved away from home and lost many things and people who felt familiar. Within the first week of college, I was invited to an APhA event, and I instantly felt the sense of belonging return. APhA has a culture of inclusivity, and this has been evident at the local, regional, and national level. Some of my favorite memories from pharmacy school include traveling to meetings in new cities with my classmates, forming connections with student pharmacists from other schools, and growing my professional network. Together, we are more knowledgeable, stronger leaders, better advocates, and we inspire one another to be our best for our patients.

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

Through APhA, I have witnessed the power of advocacy in state and national legislation and can confidently say it starts with courageously using our voices to make improvements in the lives of those around us. APhA–ASP involvement at the local and national level has instilled leadership lessons that will remain relevant in any future roles. Witnessing incredibly inspiring APhA leaders the past years has instilled in me the belief that leadership is defined by how you make others feel and I aspire to empower others on their own unique journey.

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?

Alongside Brookings County Youth Mentoring Program leadership, we organized a medication safety event at their annual Thanksgiving event for children, families, and mentors to engage in conversations surrounding safe medication use. I remember two elementary-aged children kept coming back to my station and asked very insightful questions and showed genuine interest in the topics. Through our conversation, I discovered one of the children had witnessed the impacts of medication misuse, and I knew other children and families at the event likely had shared experiences.

I later was matched to mentor this child's friend for several years afterward and aimed to show her the endless possibilities for her future and pursue any passion she discovers without fear. APhA–ASP taught me many lessons that I worked to instill in my mentee, including to live courageously, use her voice to stand up for and serve others, and to always act with kindness first.

What excites you about the profession of pharmacy?

I was initially drawn to the profession after seeing the many different roles pharmacists played in my younger sister's care growing up, and my reasons for continuing to be passionate about this profession have expanded exponentially since. I still appreciate the diverse opportunities pharmacy has to offer, particularly because it allows pharmacists to be innovative in growing the profession and as a result, the care for our patients and communities. ■

Did you know?

Digital health is a rapidly growing and advancing field that is poised to transform the delivery of health care in the United States. APhA has developed a free Practice Insights resource, 2021 DigitalHealth.Rx Summit: Thought Leaders Assembly, that considers the current health care landscape and discusses opportunities, resources needed, and next steps we can take as individuals and institutions.

This comprehensive brochure will walk you through products and solutions ranging from health apps, telehealth, digital diagnostics, and digital therapeutics to robotics and machine learning using artificial intelligence to inform treatment algorithms that are proliferating throughout the health care ecosystem.

Visit apha.us/DigitalHealth to access the free resource. ■

John Gans recognized

John Gans, PharmD, former APhA executive vice president and CEO, was announced as the recipient of the William Procter Jr. Award at Saint Joseph's University Philadelphia College of Pharmacy (PCP) during their Founders' Day event.

The William Procter, Jr., Award, presented by Edward F. Foote, PharmD, dean of PCP, was created in honor of William Procter Jr., PCP graduate, faculty member, and widely considered to be the father of American pharmacy. This award recognizes an outstanding alum who exemplifies the entrepreneurial spirit of our founding fathers and has provided outstanding service to the College and profession.

Congratulations to John Gans, PharmD '69! ■

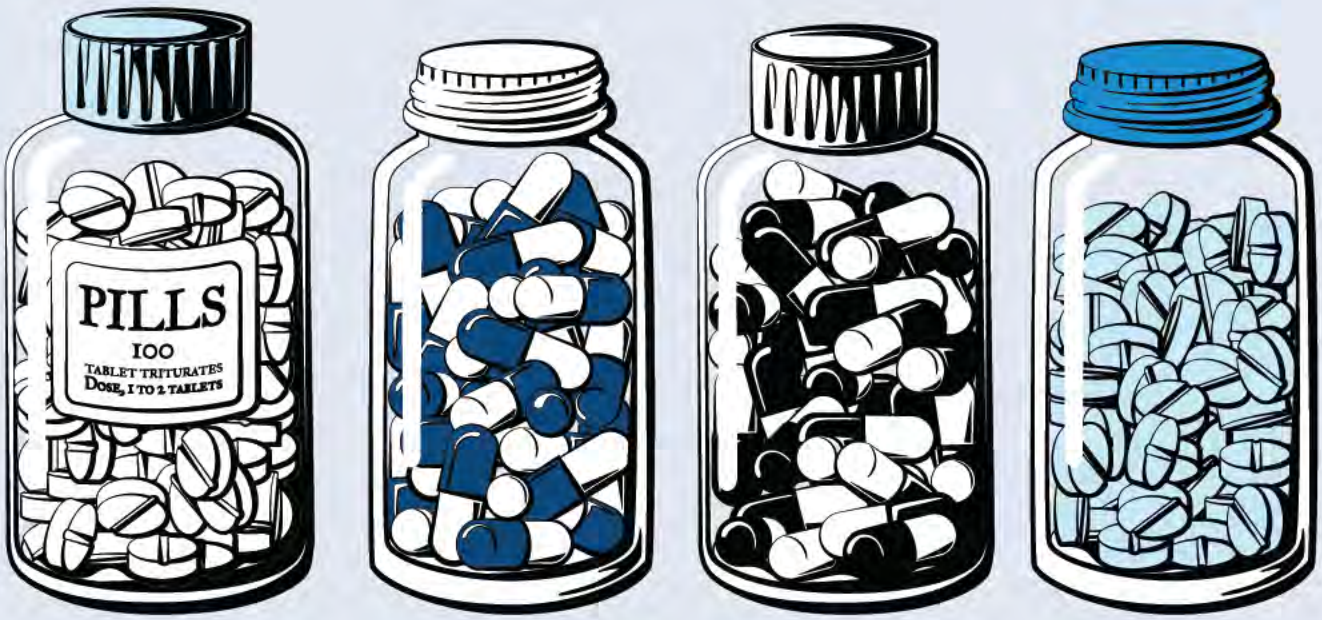
Get involved

Preceptor SIG

The APhA Preceptor Special Interest Group (SIG) serves as an interactive community where pharmacists who precept students and residents can communicate and receive feedback on precepting strategies, precepting challenges and solutions, and opportunities for preceptor growth and development.

"What I enjoy most about the Preceptor SIG is that any pharmacist in any setting can be a preceptor, so everyone brings something unique to share with other members of the SIG," said Elizabeth Yett, PharmD, assistant dean of student success at Ben and Maytee Fisch College of Pharmacy at the University of Texas at Tyler and SIG coordinator. "Our goal as a SIG is to provide resources to help each of us best develop our students into practicing pharmacists, and hopefully empower them to become preceptors themselves one day! You might be interested in joining the Preceptor SIG if you enjoy learning about best practices and tools to use when interacting with learners—from layered learning and mental health to topic discussions and difficult conversations."

Please visit apha.us/PreceptorSIG to learn more. ■



New therapeutic agents marketed in 2023: Part 1

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

FDA approved 55 new drugs in 2023. Twenty-eight (51%) of these new drugs received orphan drug designation because they are used in the treatment of patients with rare diseases. Five new therapeutic agents are considered in this review, the first in a two-part series of articles on new therapeutic agents approved in 2023: bexagliflozin (Brenzavvy–TheracosBio), sotagliflozin (Inpefa–Lexicon), zavegepant hydrochloride (Zavzpret–Pfizer), lecanemab-irmb (Leqembi–Eisai; Biogen), and fezolinetant (Veozah–Astellas).

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

Diabetes

Bexagliflozin (Brenzavvy–TheracosBio) is the fifth drug in a class of orally administered antidiabetic agents designated as sodium-glucose cotransporter 2 (SGLT-2) inhibitors, joining canagliflozin (Invokana–Janssen), dapagliflozin (Farxiga–AstraZeneca), empagliflozin (Jardiance–Boehringer Ingelheim; Lilly), and ertugliflozin (Steglatro–Merck). SGLT-2 is expressed in the proximal renal tubules and is responsible for reabsorption of the majority of the glucose filtered by the kidneys. By inhibiting SGLT-2, bexagliflozin and the other agents in this class reduce reabsorption of filtered glucose, increase urinary glucose excretion, and reduce blood glucose and A1C concentrations.

Similar to other SGLT-2 inhibitors, bexagliflozin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2D. Its effectiveness in reducing A1C concentrations has been demonstrated in studies in which it was used as monotherapy or in combination regimens with metformin, glimepiride (e.g., Amaryl), sitagliptin (Januvia), or other glucose-lowering drugs.

In the placebo-controlled study of bexagliflozin monotherapy, the reduction in A1C was 0.5% at week 24, compared with a reduction of 0.1% in patients receiving placebo. The new agent was noninferior to glimepiride and sitagliptin, but patients taking bexagliflozin lost more weight than those taking the comparator drugs. Bexagliflozin has not been directly compared with other SGLT-2 inhibitors in clinical studies. Continued studies with canagliflozin, dapagliflozin, and empagliflozin have resulted in these agents being approved to improve cardiac outcomes in patients with established CVD and T2D. Canagliflozin is also indicated to reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for heart failure in patients with T2D and diabetic nephropathy with albuminuria. Dapagliflozin and empagliflozin have also been approved to reduce the risk of CV death and hospitalization for heart failure in patients with heart failure, and also to reduce the risk of sustained decline in eGFR, end-stage kidney disease, CV death, and hospitalization in patients with chronic kidney disease at

Learning objectives

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

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

Preassessment questions

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

1. **Which of the following agents is most likely to cause UTIs as an adverse event?**
   a. Sotagliflozin
   b. Zavegepant
   c. Lecanemab
   d. Fezolinetant

2. **Which of the following agents is administered as a nasal spray?**
   a. Bexagliflozin
   b. Lecanemab
   c. Fezolinetant
   d. Zavegepant

3. **In comparing fezolinetant with estrogens, which of the following statements is correct?**
   a. Fezolinetant has been demonstrated to be more effective than estrogens.
   b. Estrogens are usually administered once a day, whereas fezolinetant is administered twice a day.
   c. Concurrent use of fezolinetant with a CYP1A2 inhibitor is contraindicated, but estrogens do not interact with CYP1A2 inhibitors.
   d. The two agents should be used concurrently for maximum effectiveness.

risk of progression. However, these are not labeled indications for bexagliflozin or ertugliflozin at the present time.

The most commonly experienced adverse events in the clinical trials of bexagliflozin include increased urination (7%), UTI (6%), and female genital mycotic infection (6%). Serious UTIs, including pyelonephritis and urosepsis, have been infrequently experienced, and patients should be advised to report signs or symptoms of UTI so that treatment can be initiated promptly. Volume depletion may result in acute kidney injury and, prior to initiating treatment, volume status should be assessed and corrected if necessary in patients with impaired renal function or low systolic BP, in older adult patients, or patients treated with diuretics.

Other precautions with the use of bexagliflozin are similar to those of the other SGLT-2 inhibitors and include monitoring in patients at risk for ketoacidosis, monitoring patients for signs and symptoms or ulcers of the lower limbs that may be associated with a greater risk of lower limb amputation, and the potential for necrotizing fasciitis of the perineum (Fournier's gangrene).

Although bexagliflozin is not likely to cause hypoglycemia, it can increase the risk of hypoglycemia when used in combination with insulin or an insulin secretagogue (e.g., a sulfonylurea). A lower dosage of the latter agents may be necessary with the use of such combination regimens.

Based on the occurrence of adverse events in animal reproduction studies, the use of bexagliflozin or the other SGLT-2 inhibitors is not recommended during the second or third trimester of pregnancy. These agents are also not recommended for use in nursing mothers. The effectiveness and safety of bexagliflozin in patients younger than 18 years have not been established; empagliflozin is the only SGLT-2 inhibitor with a labeled indication (T2D) in pediatric patients aged 10 years and older. A higher incidence of adverse events related to volume depletion has been observed in geriatric patients.

Following oral administration, bexagliflozin is primarily metabolized by uridine 5′-diphospho-glucuronosyltransferase (UGT) 1A9 to an inactive glucuronide metabolite, and to a lesser extent by CYP3A. Approximately 50% and 40% of a dose of the drug is eliminated in the feces and urine, respectively. The use of the new drug is not recommended in patients with an eGFR of <30 mL/min/1.73 m^2 or in patients with severe hepatic impairment.

The concurrent use of a UGT enzyme inducer (e.g., rifampin) may reduce the exposure and efficacy of bexagliflozin, and an additional antihyperglycemic agent may be necessary to attain glycemic control. Serum lithium concentrations may be decreased by the concurrent use of a SGLT-2 inhibitor, and concentrations of lithium should be monitored more frequently when bexagliflozin is initiated and discontinued. Because SGLT-2 inhibitors increase urinary glucose excretion and lead to positive urine glucose tests, alternative methods to monitor glycemic control should be used.

The recommended dosage of bexagliflozin is 20 mg once a day in the morning, with or without food. Treatment with the drug should be withheld for at least 3 days, if possible, prior to

Comparison with canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin

Advantages

- Is less costly.

Disadvantages

- Has not been directly compared with other SGLT-2 inhibitors in clinical studies.
- Labeled indications are more limited (compared with canagliflozin, dapagliflozin, and empagliflozin).
- Use is limited to adults (compared with empagliflozin that is also indicated for pediatric patients aged 10 years and older with T2D).

major surgery or procedures associated with prolonged fasting.

Bexagliflozin tablets are supplied in a 20 mg potency, and the tablets should not be crushed or chewed. The cost of treatment may be considerably less than with the other SGLT-2 inhibitors through an arrangement between the manufacturer and the Mark Cuban Cost Plus Drug Company.

Heart failure

Sotagliflozin (Inpefa–Lexicon) is the first dual-action SGLT inhibitor that inhibits SGLT-2 and also SGLT-1. The inhibition of SGLT-1 reduces intestinal absorption of glucose and sodium, whereas the inhibition of SGLT-2 reduces renal reabsorption of glucose and sodium. The focus of the clinical trials of sotagliflozin was to reduce the risk of heart failure and related CV events, and it has been approved to reduce the risk of CV death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure, or T2D, chronic kidney disease, and other CV risk factors. Although patients enrolled in the clinical trials had T2D, unlike the agents that selectively inhibit SGLT-2, sotagliflozin is not indicated to improve glycemic control in patients with T2D.

Sotagliflozin was evaluated in two placebo-controlled studies. In one study in patients with T2D who had been admitted to a hospital or other treatment facility for worsening heart failure, sotagliflozin was superior to placebo in reducing the risk of the primary composite endpoint of total occurrence of CV death, hospitalization for heart failure, and urgent heart failure visit (event rates per 100 patient-years of 51.3 with sotagliflozin and 76.4 with placebo). The second study was conducted in patients with T2D, chronic kidney disease, and additional CV risk factors (e.g., hypertension, dyslipidemia), and sotagliflozin was superior to placebo in reducing the risk of the primary composite endpoint noted above (event rates per 100 patient-years of 5.6 with sotagliflozin and 7.5 with placebo). However, with respect to the CV death component of the composite endpoint, the difference between sotagliflozin and placebo was not statistically significant in either of the studies.

The adverse events experienced most often in the second clinical trial with more than 10,000 patients include urinary tract infection (12%), diarrhea (8%), hypoglycemia (8%), and volume depletion (5%). Diarrhea is probably attributable to the inhibition of SGLT-1, and is not likely to occur with the use of the SGLT-2 inhibitors.

The warnings and precautions with the use of sotagliflozin are very similar to those of bexagliflozin and the other SGLT-2 inhibitors as identified in the review of bexagliflozin above. However, unlike the labeling for the SGLT-2 inhibitors, the labeling for sotagliflozin does not include a warning regarding the risk of lower limb amputation.

Comparison with canagliflozin, dapagliflozin, empagliflozin, ertugliflozin, and bexagliflozin

Advantages

- Is the first dual-action SGLT-2 and SGLT1 inhibitor.
- May be more effective in some patients with heart failure.

Disadvantages

- Has not been directly compared with other treatments in clinical studies.
- Is more likely to cause diarrhea.
- Labeled indications are more limited.

Following oral administration, the absolute bioavailability of sotagliflozin is approximately 25%. It is primarily metabolized by UGT1A9 to an inactive glucuronide metabolite. Approximately 55% and 35% of a dose of the drug is eliminated in the urine and feces, respectively. There is an increase in volume-related adverse events (e.g., hypotension, dizziness) in patients whose eGFR is <30 mL/min/1.73 m^2 and, in the clinical trials, the drug was discontinued in patients if eGFR fell below 15 mL/min/1.73 m^2 or were initiated on chronic dialysis. Dosage adjustment of sotagliflozin is not necessary in patients with mild hepatic impairment; however, exposure is significantly increased in patients with moderate or severe hepatic impairment and use is not recommended in these patients.

In addition to the interactions identified for bexagliflozin in the previous discussion, the exposure of digoxin is increased in patients treated with sotagliflozin and concurrent use should be monitored appropriately.

Volume status should be assessed, and corrected if necessary, prior to initiating treatment with sotagliflozin. The recommended initial dosage is 200 mg once a day taken not more than 1 hour before the first meal of the day. The dosage may be increased to 400 mg once a day as tolerated. Treatment should be withheld at least 3 days, if possible, prior to major surgery or procedures associated with prolonged fasting.

Sotagliflozin tablets are supplied in 200 mg and 400 mg potencies. The tablets should be swallowed whole, and should not be cut, crushed, or chewed.

Migraine

Calcitonin gene-related peptide (CGRP) is a neuropeptide that is distributed primarily in the central and peripheral nervous systems and acts as a vasodilator. It is involved in the transmission of pain impulses, and ele-

vated concentrations have been associated with migraine attacks. Since 2018, eight CGRP antagonists have been marketed, four of which are monoclonal antibodies, that are administered parenterally. Erenumab (Aimovig–Amgen), fremanezumab (Ajovy–Teva), and galcanezumab (Emgality–Lilly) are administered subcutaneously, and eptinezumab (Vyepti–Lundbeck) is administered intravenously, for preventive treatment of episodic and chronic migraines. Three orally administered CGRP antagonists have been approved for migraine indications. Ubrogepant (Ubrelvy–AbbVie) is indicated for the acute treatment of migraine, atogepant (Qulipta–AbbVie) is indicated for the preventive treatment of episodic migraine, and rimegepant (Nurtec ODT–Pfizer) for both acute treatment and preventive treatment (but in different dosage regimens). Zavegepant hydrochloride (Zavzpret–Pfizer) is the first CGRP antagonist to be approved for intranasal administration.

Zavegepant is administered as a nasal spray for the acute treatment of migraine with or without migraine in adults, and it provides a faster onset of action than the CGRP antagonists that are administered orally. It was evaluated in two placebo-controlled trials in which the coprimary endpoints were pain freedom and most bothersome symptom (MBS; e.g., photophobia) freedom at 2 hours after a single dose. Pain freedom was experienced by 24% and 23% of the patients treated with zavegepant in the two studies, compared with 15% and 16% of those receiving placebo. Relief of pain occurred as early as 15 minutes following administration. MBS freedom was experienced by 40% and 42% of patients treated with zavegepant, compared with 31% and 34% of those receiving placebo. The CGRP antagonists are less effective than the triptans (e.g., sumatriptan [e.g., Imitrex]) for the acute treatment of migraine, but the triptans are contraindicated in patients with certain CV and other disorders, and their labeling includes numerous warnings that are applicable to their use.

Comparison with ubrogepant, rimegepant, and atogepant

Advantages

- Is the first CGRP antagonist to be administered intranasally.
- Has a faster onset of action.
- May be less likely to interact with CYP3A4 inhibitors and inducers.

Disadvantages

- Has not been directly compared with other treatments in clinical studies.
- Labeled indications do not include preventive treatment with migraine (compared with rimegepant and atogepant).

The most commonly experienced adverse events in the clinical studies include taste disorders (18%), nausea (4%), nasal discomfort (3%), and vomiting (2%). Hypersensitivity reactions, including facial swelling and urticaria, occurred in less than 1% of the patients treated with zavegepant. There is very little information regarding the use of zavegepant during pregnancy, but the results of studies in animals suggest that it is not likely to be associated with adverse developmental effects. The effectiveness and safety of the drug in pediatric patients have not been established.

Following administration of zavegepant as a nasal spray, the absolute bioavailability is approximately 5%. It is primarily metabolized by CYP3A4 and to a lesser extent by CYP2D6, and is excreted mostly via the biliary/fecal route. The use of zavegepant has not been adequately studied in patients with severe hepatic impairment or in patients with a creatinine clearance less than 30 mL/min, and use in these patients should be avoided.

Zavegepant is a substrate of the organic anion transporting polypeptide (OATP) 1B3 and sodium taurocholate cotransporting polypeptide (NTCP) transporters, and concurrent use of agents (e.g., rifampin) that inhibit these transporters may result in a significant increase in zavegepant exposure. Concomitant use with inducers of these transporters should also be avoided because of the possible reduction in exposure of the new agent. An intranasal decongestant may reduce the effectiveness of zavegepant, and concurrent use should be avoided. However, if concurrent use can't be avoided, the intranasal decongestant should be administered at least one hour after zavegepant.

The recommended dosage of zavegepant is 10 mg given as a single spray in one nostril as needed. The maximum dose in a 24-hour period is 10 mg (one spray). The safety of treating more than eight migraines in a 30-day period has not been established. Zavegepant hydrochloride is supplied in a unit-dose nasal spray device in a quantity that provides 10 mg of zavegepant that is delivered in a single spray. The product is sup-

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

plied in cartons containing six disposable nasal spray devices.

Alzheimer disease

Although progress has been made in identifying pathophysiologic features of Alzheimer disease, differences of opinion continue to exist regarding the importance of these characteristics and potential treatments. The identification of accumulated amyloid beta plaques in the brains of patients with Alzheimer disease has resulted in a strong focus in research studies of agents that reduce the number of these plaques.

Aducanumab (Aduhelm–Biogen) is a humanized monoclonal antibody that is directed against forms of amyloid beta and was approved in 2021 as the first drug that is directed against the underlying pathophysiology of the disease. It is administered intravenously in patients with mild cognitive impairment or mild dementia stage of disease. Aducanumab was approved by FDA under the provisions of its accelerated approval program based on reduction of amyloid beta plaques. However, because of serious questions about the clinical trials and effectiveness, FDA's decision to provide accelerated approval, the cost, restricted Medicare coverage, and the accelerated approval of a second anti-amyloid beta drug, aducanumab did not receive full approval by FDA. On January 31, 2024, Biogen announced that it was discontinuing marketing of aducanumab, as well as clinical studies that had been ongoing.

Lecanemab-irmb (Leqembi–Eisai; Biogen) is a humanized monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta, and received accelerated approval by FDA on January 6, 2023, for I.V. administration in patients with Alzheimer disease. Treatment should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the patient population in which treatment was initiated in clinical trials. The presence of amyloid beta pathology should be confirmed prior to initiating treatment. Based on continuing studies in which lecanemab slowed cognitive and functional decline, FDA granted traditional (full) approval on July 6, 2023. CMS has announced that it will cover the drug in appropriate settings that also support the collection of real-world information in a registry for the purpose of studying its usefulness.

Comparison with aducanumab

Advantages

- Has provided modest slowing of cognitive decline.
- Has received full FDA approval (aducanumab received accelerated approval based on reduction of amyloid beta plaques, but marketing has been subsequently discontinued).

Disadvantages

- Is administered more frequently (compared with every 4 weeks with aducanumab).

Lecanemab was evaluated in a placebo-controlled study in which the primary efficacy outcome was change from baseline at 18 months in the Clinical Dementia Rating Scale Sum of Boxes (CDR-SB). Key secondary endpoints included change from baseline at 18 months in the following measures: amyloid positive emission tomography using Centiloids, Alzheimer's Disease Assessment Scale–Cognitive Subscale 14 (ADAS–Cog14), and Alzheimers Disease Cooperative Study–Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL). Lecanemab demonstrated statistically significant changes in the primary and all key secondary endpoints from baseline compared to placebo. It modestly slowed cognitive decline but did not stop or reverse it. Reduction in amyloid beta plaques was also statistically significantly greater with lecanemab.

In the analyses of subgroups of patients in the study, the differences between lecanemab and placebo were not statistically significant in female patients or in patients who are carriers of the apolipoprotein E4 (APOE4) allele.

The most commonly experienced adverse events in patients in the clinical trial include infusion-related reactions (26%), amyloid related imaging abnormality with hemosiderin deposition (ARIA-H; including microhemorrhage and superficial siderosis; 14%), amyloid related imaging abnormality-edema (ARIA-E; observed on MRI as brain edema or sulcal effusions; 13%), headache (11%), superficial siderosis of the central nervous system (6%), rash (6%), and nausea/vomiting (6%). If infusion-related reactions occur, the infusion rate may be reduced, or the infusion discontinued. With subsequent doses, premedication with antihistamines, NSAIDs, or corticosteroids should be considered.

The risk of ARIA is the subject of a boxed warning in the labeling for lecanemab. ARIA is usually asymptomatic, although rarely serious, and life-threatening events (e.g., seizure, status epilepticus) can occur. Serious intracerebral hemorrhages greater than 1 cm have been reported. Patients who are APOE4 homozygotes have a higher incidence of ARIA, compared to heterozygotes and noncarriers. APOE4 status should be determined prior to initiation of treatment to assess the risk of developing ARIA.

Lecanemab injection is supplied in single-dose vials containing 500 mg/5 mL and 200 mg/2 mL. The vials should be stored in a refrigerator in the original carton to protect from light. A recent baseline brain MRI should be obtained prior to initiating treatment.

The recommended dosage of lecanemab is 10 mg/kg and the dose is diluted in 250 mL of 0.9% sodium chloride injection. The dilution is administered as an I.V. infusion over approximately 1 hour once every 2 weeks via a terminal low-protein binding 0.2 micron in-line filter. An MRI should be obtained prior to the 5th, 7th, and 14th infusions. If radiographically observed ARIA occurs, treatment recommendations are based on type, severity, and presence of symptoms.

Menopause

Women usually experience menopause between ages 45 and 55 years. The production of estrogens and progesterone diminishes, resulting in vasomotor

symptoms (VMS) including hot flashes in approximately 80% of menopausal women. Hot flashes can include periods of sweating, flushing, and chills lasting several minutes. Estrogens are the most effective treatment for VMS but these agents, as well as the combination product Duavee, which contains conjugated estrogens and bazedoxifene (a selective estrogen receptor modulator), cause estrogen-related adverse events that result in risk and/or intolerance for some women. A low-dose formulation of paroxetine mesylate (Brisdelle) was the first nonhormonal treatment to be approved for the management of VMS. Other agents have been used off-label, and black cohosh and phytoestrogens have also been widely used.

Neurokinin B (NKB) binds on the kisspeptin/neurokinin B/dynorphin (KNDy) neurons to modulate neuronal activity in the thermoregulatory center. These neurons are stimulated by NKB and inhibited by estrogen at neurokinin 3 (NK3) receptors. When estrogen concentrations are reduced during menopause, NKB activity increases, resulting in VMS.

Fezolinetant (Veozah–Astellas) is a NK3 receptor antagonist and is the second nonhormonal treatment to be approved for women who experience VMS during menopause. It is specifically indicated for the treatment of moderate to severe VMS due to menopause. It was evaluated in two placebo-controlled clinical trials in women who had a minimum average of seven moderate to severe VMS per day. The coprimary efficacy endpoints for both trials were the mean change from baseline in moderate to severe VMS frequency and severity at weeks 4 and 12. Data from each trial demonstrated statistically significant and clinically meaningful (2 or more hot flashes over 24 hours) reduction from baseline in the frequency of VMS, and a statistically significant reduction from baseline in the severity of moderate to severe VMS over 24 hours. In each trial after the first 12 weeks, the women on placebo were rerandomized to fezolinetant for a 40-week extension study (total of 52 weeks) and the improvements were maintained.

Comparison with estrogens

Advantages

- Has a unique mechanism of action (is the first NK3 receptor antagonist to be approved).
- Is better tolerated by some patients.

Disadvantages

- Is more likely to cause hepatic adverse events.
- Concurrent use with a CYP1A2 inhibitor is contraindicated.
- Has not been directly compared with estrogens in clinical studies.

The adverse events most often reported in the clinical trials include abdominal pain (4%), diarrhea (4%), insomnia (4%), back pain (3%), hot flush (3%), and hepatic transaminase elevation (2%). One case of endometrial hyperplasia and one case of endometrial malignancy were identified in the studies. The exposure of fezolinetant is increased in women with hepatic impairment and its use is contraindicated in women with known cirrhosis. It has not been studied in women with severe hepatic impairment. Prior to initiating therapy, patients should be evaluated for hepatic function and injury, including serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), and serum bilirubin (total and direct). If serum transaminase concentration is equal to or exceeds two times the upper limit of normal, treatment should not be started. In women who are appropriate candidates for treatment, follow-up evaluations of hepatic transaminase concentration should be performed at 3, 6, and 9 months after starting therapy and when symptoms (e.g., nausea, vomiting, yellowing of the skin or eyes) suggest liver injury.

Following oral administration, fezolinetant is primarily metabolized by CYP1A2 and to a lesser extent by CYP2C9 and CYP2C19. Approximately 75% of a dose and 15% of a dose is excreted as metabolites in the urine and feces, respectively. The new agent is contraindicated in women with severe renal impairment or end-stage renal disease (eGFR <15 mL/min/1.73 m^2).

As a substrate of CYP1A2, the maximum serum concentration and exposure of fezolinetant are markedly increased by CYP1A2 inhibitors, and concurrent use with strong (e.g., fluvoxamine), moderate (e.g., mexiletine), and weak (e.g., cimetidine) CYP1A2 inhibitors is contraindicated. No clinically significant differences in fezolinetant exposure were observed in smokers (moderate CYP1A2 inducers).

The recommended dosage of fezolinetant is 45 mg once a day. Tablets are supplied in a 45 mg potency and should not be cut, crushed, or chewed. ■

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To obtain 1 hour of CPE credit for this activity, complete the CPE exam and submit it online at www.pharmacist.com/education. A Statement of Credit will be awarded for a passing grade of 70% or better. You have two opportunities to successfully complete the CPE exam. Pharmacists and technicians who successfully complete this activity before April 1, 2027, can receive credit. Your Statement of Credit will be available online immediately upon successful completion of the CPE exam.

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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. **Which of the following acts as a neurokinin 3 receptor antagonist?**
   a. Sotagliflozin
   b. Zavegepant
   c. Lecanemab
   d. Fezolinetant

2. **Which of the following agents has a labeled indication to improve glycemic control in adults with T2D?**
   a. Sotagliflozin
   b. Zavegepant
   c. Bexagliflozin
   d. Fezolinetant

3. **Which of the following agents is most likely to cause UTIs as an adverse event?**
   a. Sotagliflozin
   b. Zavegepant
   c. Lecanemab
   d. Fezolinetant

4. **With which of the following agents were the differences between the drug and placebo not statistically significant in female patients?**
   a. Bexagliflozin
   b. Lecanemab
   c. Zavegepant
   d. Fezolinetant

5. **Which of the following agents is administered as a nasal spray?**
   a. Bexagliflozin
   b. Lecanemab
   c. Fezolinetant
   d. Zavegepant

6. **Which of the following statements is correct regarding bexagliflozin?**
   a. Its use is not recommended during the second or third trimester of pregnancy.
   b. Constipation is the most commonly experienced adverse event.
   c. It is administered twice a day.
   d. It is eliminated in unchanged form in the urine.

7. **Which of the following statements is correct regarding sotagliflozin?**
   a. It reduces the activity of rifampin.
   b. Inhibition of SGLT-1 is considered the reason for diarrhea being a common adverse event.
   c. It is primarily metabolized via the CYP3A4 pathway.
   d. It is administered once a day in the evening.

8. **Which of the following statements is correct regarding zavegepant?**
   a. It acts as a vasoconstrictor.
   b. It should be administered with food.
   c. Concurrent use with a nasal decongestant is best avoided.
   d. It is available in immediate-release and extended-release formulations.

9. **Which of the following statements is correct regarding lecanemab?**
   a. Hepatic adverse events are the most important risk associated with its use.
   b. Transaminase concentrations should be performed at 3, 6, and 9 months following initiation of therapy.
   c. Its use should be avoided in patients with hepatic or renal impairment.
   d. The recommended dosage is 10 mg/kg once every 2 weeks.

10. **In comparing fezolinetant with estrogens, which of the following statements is correct?**
    a. Fezolinetant has been demonstrated to be more effective than estrogens.
    b. Estrogens are usually administered once a day, whereas fezolinetant is administered twice a day.
    c. Concurrent use of fezolinetant with a CYP1A2 inhibitor is contraindicated, but estrogens do not interact with CYP1A2 inhibitors.
    d. The two agents should be used concurrently for maximum effectiveness.

Across

7 Microorganisms that can cause disease
8 Injury that can be caused by an I.V. line
10 Kind of cooking oil
11 Brand name of amygdalin
12 _____ implants can improve hearing for some patients
13 Common allergic reaction to penicillin
15 This is necessary to practice pharmacy
17 Flabby, like a muscle
20 Memory loss can be an early _____ of dementia
22 Often used to treat conjuntivitis
25 Immunity developed from a vaccine or exposure to a disease
26 With 27 across and 9 down, subject of this month's cover story
27 See 26 across
28 Organ that controls all bodily function

Down

1 Cephalosporin antibiotic usually given by injection
2 Blended beverage that contains fruit
3 Bacterial infection that can cause severe dehydration...and death
4 Brainy, intellectual
5 Can help prevent scurvy
6 Small solid round masses of medicine that you swallow without chewing
9 See 26 across
14 Cofactor necessary for serotonin synthesis
16 Group of symptoms that occur together and suggest the presence of a certain disease
18 The "C" in CAD
19 Fibrous connective tissues that attach muscle to bone
21 Common prebiotic
23 Ova
24 Mock or ridicule, with "at"

Solution is available online at pharmacytoday.org.