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

RURAL AMERICA NEEDS ITS PHARMACISTS

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CDC recommends new drug to protect infants from RSV

FDA approved nirsevimab-alip (Beyfortus—Sanofi/AstraZeneca) in July 2023. A few weeks later, on August 3, 2023, CDC's ACIP voted unanimously to recommend the broad use of the new drug in infants and high-risk children for protection against respiratory syncytial virus (RSV).

Nirsevimab-alip is the first-ever drug to safeguard infants against RSV. CDC advisers who recommended its use described nirsevimab as a significant breakthrough against a respiratory disease that causes the deaths of as many as 300 children a year in the United States and is the primary cause of hospitalization among infants in the United States.

FDA said it approved the drug based on studies indicating that it safely prevented severe RSV-associated lower respiratory tract infections.

Although nirsevimab-alip is not a vaccine, it has a similar goal. The drug gives infants antibodies to neutralize the virus before their immune systems are sufficiently mature enough to combat the pathogens.

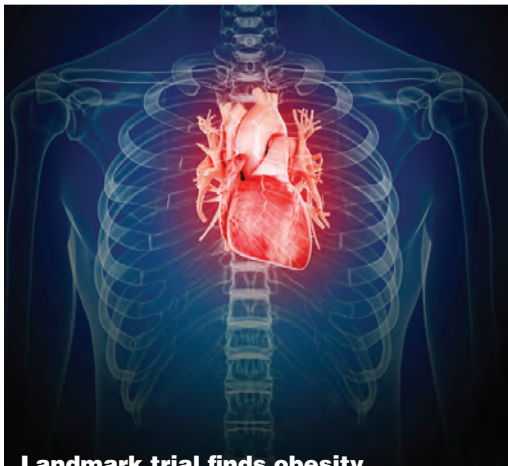
Nirsevimab-alip will usually require a single dose. Under FDA approval, infants can receive nirsevimab-alip at the start of an RSV season or during it if the season has already commenced. Children who are at high risk for developing severe RSV can receive a second dose for a second RSV season if they are younger than 2 years old, according to Sanofi.

The company expects to make nirsevimab-alip available in time for this year's RSV season.

ACIP recommended the drug be offered to all infants born during the RSV season or to those who are less than 8 months old as they enter their first RSV season. They also recommended that high-risk children ages 8 months to 19 months receive a second dose of nirsevimab prior to their second RSV season.

ACIP's third recommendation was to include nirsevimab in the Vaccines for Children program, even though the drug is not a vaccine. Inclusion in the program ensures that children of parents without health insurance can receive the drug at no cost.

Sanofi indicated to ACIP it will charge $495 per dose, which is costlier than a typical vaccine. ■



Landmark trial finds obesity drug cuts CVD risk significantly

New findings from the SELECT trial indicate that semaglutide (Wegovy) reduces the risk of major heart complications—heart attacks, strokes, and CV deaths—by 20%. The 5-year randomized trial of approximately 17,500 patients is the first to demonstrate that an obesity drug can have long-term CV benefits.

The trial included participants 45 years and older who were overweight or had obesity and who had established CVD.

Novo Nordisk said the drug seemed to have a "safe and well-tolerated profile" compared with prior studies of semaglutide. The company said it would offer detailed results from the trial at a conference later this year.

The drug's high price, however, makes insurance coverage uncertain, and it's unclear whether the new trial results may convince health insurers and employers to cover the therapy. ■

Disparities persist in Black adults' stroke risk

According to the American Heart Association (AHA), significant disparities for stroke risk factors exist between Black adults and non-Black adults who have had a stroke.

Research findings published in AHA's *Stroke* on August 3, 2023, found that major differences were seen at enrollment in the study for Black participants compared to non-Black participants. Black adults had a younger age (57.5 years old vs. 61 years old), and they had more incidences of high BP (95.2% vs. 87.5%), more prevalence of T2D (52.9% vs. 39.7%), higher average diastolic BP (82.4 mm Hg vs. 79.5 mm Hg), and lower physical activity PACE scores (2.7 vs. 3.3). A PACE score of 4 or above is considered moderately active and within target range.

"Modifiable stroke risk factor differences between Black and non-Black adults were found at enrollment; however, our study found these disparities may be resolved by tailoring care to include lifestyle coaching, medication alterations or additions if appropriate, access to routine health care support and regular physician follow-up," said study coauthor Ashley Nelson, DO, in a press statement. "Intense risk factor management has an important role in improving or eliminating these risk factor disparities in Black adults."

However, after 1 year of intensive medical intervention, some of the risk factors that increase the risk of stroke were reduced in the Black adults, according to research. Specifically, the average diastolic BP in Black patients dropped to 74.7 mm Hg compared to 75.5 mm Hg in all other participants, and the average PACE score increased among Black patients to 4.2 from 2.7. In comparison, the average PACE score among non-Black adults was 4.1, and the percentage of diuretic medication use doubled in Black adults. Researchers speculate that the increased use of thiazide diuretics may explain the notable decrease in average diastolic BP.

For the analysis, researchers examined health data from the SAMMPRIS randomized controlled trial conducted from 2008 to 2011 at 50 sites within the United States. They evaluated medication use and vascular risk factors, such as systolic BP, diastolic BP, LDL, blood glucose levels, and physical activity of Black and non-Black adults with a recent stroke event.

The non-Black participant group included white, Asian, and Hispanic adults, who were measured collectively.

The authors note that their research raises questions about other factors beyond physiology, medications, and regular follow-up that may help to reduce these disparities even further.

"Many different approaches are needed to reduce and eliminate these disparities in Black adults," Nelson said. "Access to health care, lifestyle coaching, early follow-up, and administration of appropriate medications after stroke may help to resolve it, but not wholly in terms of overall risk and all of the baseline disparities." ■

Is PPI use connected to dementia risk?

Prolonged use of PPIs, which are designed to control acid reflux and other GI disorders, may raise the risk of dementia, according to a study published August 9, 2023, in *Neurology.*

The study included 5,712 older adults who were dementia-free at baseline, defined as visit 5 in the ongoing ARIC study.

The researchers reported that participants in the ARIC cohort who used PPIs for more than 4.4 years had a higher risk of dementia compared with those reporting no PPI use.

The participants were placed into four groups: those not using PPIs, those using them for up to 2.8 years, those using them for 2.8 to 4.4 years, and those using them for more than 4.4 years. Overall, 1,490 participants used PPIs, ranging from a minimum cumulative PPI use of 112 days to a maximum use of 20.3 years. Median use was 3.8 years, while mean use was 4.4 years. Over a median of 5.5 years, 585 people developed dementia. Only the participants who used PPIs for more than 4.4 cumulative years prior to visit 5 had a higher risk of developing dementia compared with those not using PPIs.

In a secondary analysis, the researchers examined the relationship between PPIs and dementia with histamine-2 receptor antagonists (H2Ras) as an active comparator. The results were similar, as more than 4.4 cumulative years of exposure to PPIs were associated with greater dementia risk compared with H2Ras. However, there was no association with use for shorter durations or current use. ■

Few adults receive medication for opioid use disorder

A study published August 7, 2023, in *JAMA Network Open* found that as drug overdose deaths have reached unprecedented levels in the United States, evidence-based treatments for substance use are severely underused.

The study, led by researchers at the National Institute on Drug Abuse and the National Center for Injury Prevention, found that only about one-third of adults with opioid use disorder (OUD) received any type of treatment for substance use, and only about one in five received medication to treat OUD.

The study focused on data from more than 47,000 adults who participated in the 2021 National Survey on Drug Use and Health, which is sponsored by the Substance Abuse and Mental Health Services Administration.

An estimated 2.5 million adults nationwide have OUD, for which FDA has approved therapies such as methadone, buprenorphine, and naltrexone.

The study noted significant differences for those who received medication to treat OUD. Men with OUD were six times more likely than women to receive OUD treatment, while white adults were 14 times more likely to receive treatment compared with Black adults.

Adults living in nonurban areas and unemployed adults were also less likely to receive OUD medications.

In addition, the study backs previous findings that indicated the use of telehealth improved treatment rates. Individuals who received substance use treatment through telehealth were nearly 40 times more likely to receive medications for OUD compared with those who did not receive telehealth treatment, according to the researchers. ■

CDC: MMR vaccinations fall for children

According to new CDC data, the rate of vaccinations against measles, mumps, and rubella (MMR) for kindergarteners has fallen below the optimum target rate of 95% for the second year in a row, declining to 93%.

"While this is a small decline, this is the lowest MMR rate reported in almost a decade and leaves approximately 250,000 school children unvaccinated and unprotected against measles, one of the world's most contagious viruses," a recent Kaiser Family Foundation brief said.

Vaccine hesitancy is likely playing a role.

The United States' Healthy People 2030 target of 95% reflects the coverage rate deemed high enough to ensure herd immunity against community transmission. MMR vaccinations are regarded as critical because of the contagious nature of measles.

CDC advises that the initial dose of MMR vaccines be administered at the age of 12 months to 15 months, with a second dose given at 4 years to 6 years old. ■

Hospital pharmacists say drug shortages are affecting care

New survey findings from the American Society of Health-System Pharmacists (ASHP) showed that roughly 99% of health-system pharmacists said they are experiencing drug shortages. Nearly one-third of the respondents said the current shortages are "critically impactful," causing facilities to delay, ration, or cancel procedures or treatments.

More than 1,000 ASHP members responded to the internal survey between late June and mid-July 2023. According to the findings, chemotherapy drugs are among the most pressing shortages, with 57% of pharmacists saying this category had a direct effect on patient care.

A separate survey released in June 2023 from major cancer centers found that 93% were unable to locate sufficient carboplatin, and 70% experienced shortages of cisplatin. Both are frequently used in combination to treat many forms of cancer.

Meanwhile, the ASHP survey also found that shortages of corticosteroids and other hormonal drugs, in addition to oral liquids such as amoxicillin, have had major effects on patient care.

More than 40% of health-system pharmacists said they have had to delay or cancel treatments or procedures because of a drug shortage. Furthermore, 85% said they have had to ration drugs, while 97% said they had to use therapeutic alternatives.

Approximately 85% of the pharmacists also said they would be willing to spend more for drug products from companies vetted by a quality recognition program. ■

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CPE

46 **Responding to medication errors using a just culture approach**

Ronald Zentz and Georgia Reiner

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Take the Crossword Challenge

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See solution at pharmacytoday.org

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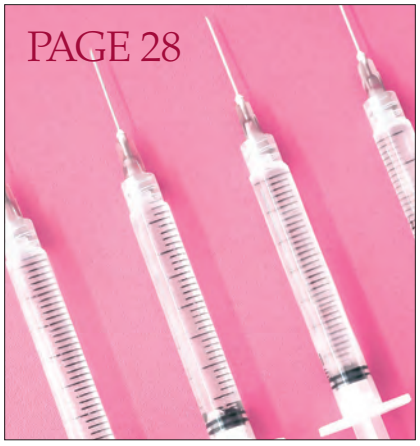
Drugs & Diseases



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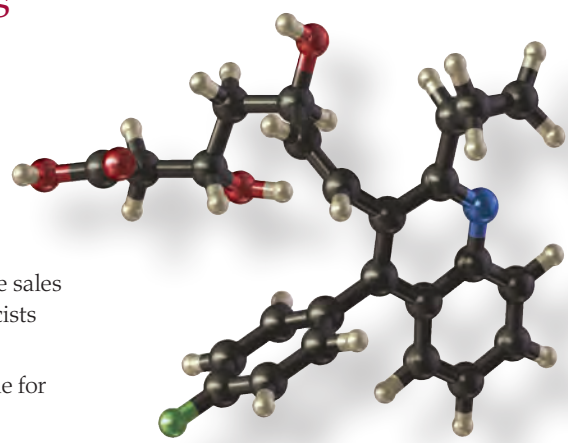


Rural pharmacists are unsung heroes for patient care

I lived in a rural area for nearly 20 years. At first, there were four pharmacies within about a 20-mile radius. By the time I moved away in 2020, there were just two pharmacies left. When my children were young, the pediatrician's office was more than an hour's drive away, so we relied heavily on our pharmacist.

My situation was not unusual. About 15% of the U.S. population lives in rural areas. Most of these individuals face daunting challenges to accessing much-needed care.

The cover story for this issue of *Pharmacy Today* takes a close look at rural pharmacies and the pharmacists who are going above and beyond to care for their patients. Allison Reichert, PharmD, vice president of operations at Bode Drugs in Vienna, IL, says many of her patients have her cell phone number, while her pharmacy offers an emergency after-hours telephone line. Among other specialized services, she takes vaccines to the community, offering influenza, COVID-19, pneumonia, and shingles shots in local businesses and assisted living facilities.

Being accessible to patients is essential to her practice. "In a rural area, a lot of patients don't have transportation. It might be 35 miles to the doctor, so that's something to keep in mind," says Reichert.

In this issue of *Pharmacy Today,* you'll also find the latest info on new drug approvals including FDA's first OTC oral contraceptive approval, learn how probiotics may bolster antidepressant effects, and get answers to your patients' questions about the potential dangers of aspartame. Get the latest on changes in insulin prices as new products hit the market and catch up with your CPE credit with this month's article on approaches to responding to medication errors.

There is no easy solution to many factors driving the closure of rural pharmacies, which include low-volume purchasing, slim profit margins, insurance practices, and a limited pharmacy workforce. According to the University of Iowa's Rural Policy Research Institute, more than 1,000—or nearly 20%—of the nation's independent rural pharmacies closed between 2003 and 2018, leaving 630 communities without an independent or chain community pharmacy. Fortunately, we are seeing a rise in nondispensing pharmacy services such as point-of-care testing and treatment and vaccinations. Although these alone won't solve the ongoing problem, hopefully services like these can provide a boost for pharmacists and patients in rural areas.

Have a great *Today*!

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

Incivility in pharmacy

Pharmacists have unfortunately been on the receiving end of some tough situations. These include patients screaming at us at the counter, nurses cursing us under their breath on the unit, and even worse—a patient pulling a gun and demanding drugs or money. Incivility toward pharmacy personnel has gotten out of hand.

Unpacking the emotions of difficult experiences takes time. And here's the thing: unpacking means not internalizing. It means that when we have an experience in life that leaves us numb, we must find a place and space where we can talk about it. For some, it's a licensed professional counselor; for others, it's a good friend; for yet others, the outlet is a blog or social media. Every person has their own path to healing.

Unpacking also means not putting things back in the box. So often, the hindrance to healing from a difficult time or trauma is that we talk about our issue, and rather than leaving that hurtful situation or letting that feeling or past trauma go, we pick it back up, reinternalize it, and then allow it to own us for another day.

I've done this a million times. Sometimes those box lids open and close too fast for me to let go completely, and past negative experiences get replayed in my head over and again.

The thing about trauma in our lives is that we're not the only ones who go through this. We might feel alone in the moment, but I can assure you that you are not alone despite the fact that we all have different life experiences.

We can't unpack and let go because the incivility keeps happening. The patient is not always right. Colleagues shouldn't talk to each other in condescending tones. Boundaries and bright lines need to be enforced.

This American Pharmacists Month, APhA is focusing on bolstering consumer confidence in pharmacists and an awareness that kindness and courtesy are the hallmark of a great partnership with pharmacists to ensure optimal care.

While we can't take away the trauma of past events or experiences, APhA is dedicated to working with consumer organizations, the media, other health care professionals, and employers to provide a safe environment to meet patients' needs and reduce the risk of future events.

As we embark on a month dedicated to celebrating pharmacy professionals, I want to give you a word of encouragement. You are making a difference. Even if the negative noise around you is loud, you do have a purpose. Here at APhA we see you and we support you. We will continue to advocate for you every day. For every pharmacist. For all of pharmacy. ■

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

NEW DRUGS

AVACINCAPTAD PEGOL INTRAVITREAL SOLUTION
(Izervay—Iveric Bio)

Drug class: Izervay is a complement inhibitor.

Indication: Izervay is indicated for the treatment of geographic atrophy secondary to age-related macular degeneration.

Recommended dosage and administration: The recommended dose for Izervay is 2 mg (0.1 mL of 10 mg/mL solution) administered by intravitreal injection to each affected eye once monthly for up to 12 months.

Common adverse effects: The most common adverse reactions were conjunctival hemorrhage, increased intraocular pressure, blurred vision, and neovascular age-related macular degeneration.

Warnings and precautions: Izervay is contraindicated in ocular or periocular infections and active intraocular inflammation. Endophthalmitis and retinal detachments may occur with use.

PALOVAROTENE
(Sohonos—Ipsen Inc.)

Drug class: Sohonos is a retinoid.

Indication: Sohonos is indicated for reduction in the volume of new heterotopic ossification in adults and children aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva.

Recommended dosage and administration: Obtain a negative pregnancy test in females of reproductive potential before initiation of Sohonos. The recommended dosage includes a chronic daily dose, which can be increased for flare-up symptoms. For adults and pediatric patients 14 years and older, the recommended dosage is 5 mg once daily, with an increase in dose at the time of flare-up to 20 mg once daily for 4 weeks, followed by 10 mg once daily for 8 weeks for a total of 12 weeks. For pediatric patients under 14 years, the recommended dosage is weight-adjusted for daily and flare-up dosing, with the daily dosage ranging from 2.5 mg to 5 mg. Take Sohonos with food, preferably at the same time each day. Reduce the dose in the event of adverse reactions as appropriate.

Common adverse effects: The most common adverse reactions are dry skin, dry lips, arthralgia, pruritis, pain in extremities, rash, alopecia, erythema, headache, back pain, skin exfoliation, nausea, musculoskeletal pain, myalgia, dry eye, hypersensitivity, peripheral edema, and fatigue.

Boxed warning: Sohonos is contraindicated in pregnancy because of the risk of teratogenicity. To minimize fetal exposure, Sohonos is to be administered only if conditions for pregnancy prevention are met. Sohonos causes premature epiphyseal closure in growing pediatric patients with fibrodysplasia ossificans progressiva, so close monitoring is recommended.

Warnings and precautions: Sohonos is contraindicated in pregnancy and hypersensitivity to retinoids or any component of Sohonos. Premature epiphyseal closure occurred with Sohonos. Assess baseline skeletal maturity before Sohonos therapy and monitor linear growth in growing pediatric patients. Dry skin, dry lips, pruritis, rash, alopecia, erythema, skin exfoliation, and dry eye occurred with Sohonos. Prevent or treat with skin emollients, sunscreen, and artificial tears. Dosage reduction may be required in some patients. Decreased vertebral bone mineral content and bone density may occur. Assess for spinal fracture periodically using radiologic methods. Depression, anxiety, mood alterations, and suicidal thoughts and behaviors have occurred in patients taking Sohonos. Contact a health care provider if new or worsening symptoms develop in patients treated with Sohonos. Night blindness may occur and make driving at night hazardous. Avoid concomitant use of strong or moderate CYP3A4 inhibitors as well as grapefruit, pomelo, or juices containing these fruits, as this may increase Sohonos exposure. Avoid concomitant use of strong or moderate CYP3A4 inducers, as this may decrease Sohonos exposure. Taking Sohonos concomitantly with vitamin A may cause additive effects. Avoid concomitant use of tetracyclines with Sohonos. No clinically significant drug interaction is expected with concomitant use of systemic corticosteroids.

ZURANOLONE
(Zurzuvae—Sage Therapeutics)

Drug class: Zurzuvae is a neuroactive steroid gamma-aminobutyric acid A receptor positive modulator.

Indication: Zurzuvae is indicated for the treatment of postpartum depression in adults.

Recommended dosage and administration: The recommended dosage is 50 mg orally once daily in the evening for 14 days. Dosage may be reduced to 40 mg once daily if central nervous system (CNS) depressant effects occur. Zurzuvae should be administered with a fat-containing food. Zurzuvae can be used alone or as an adjunct to oral antidepressant therapy. In severe hepatic impairment, the recommended dosage is 30 mg orally once daily in the evening for 14 days. In moderate or severe renal impairment, the recommended dosage is 30 mg orally once daily in the evening for 14 days.

Common adverse effects: The most common adverse reactions were somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and UTI.

Boxed warning: Zurzuvae causes driving impairment due to CNS depressant effects. Advise patients not to drive or engage in other potentially hazardous activities until at least 12 hours after administration. Patients may not be able to assess their own driving competence or the degree of impairment caused by Zurzuvae.

Warnings and precautions: Zurzuvae can cause CNS depressant effects such as somnolence and confusion. If patients develop CNS depression, consider dosage reduction or discontinuation of Zurzuvae. Consider changing the therapeutic regimen, including discontinuing Zurzuvae, in patients whose postpartum depression worsens or who experience emergent suicidal thoughts and behaviors. Zurzuvae may cause fetal harm. Advise patients of the potential risk to an infant exposed to Zurzuvae in utero.

Advise patients of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 1 week after the final dose. Concomitant use with other CNS depressants may increase impairment of psychomotor performance or CNS depressant effects. If use with another CNS depressant is unavoidable, consider dosage reduction. Concomitant use with strong CYP3A4 inhibitors may increase the risk of Zurzuvae-associated adverse reactions. Reduce the Zurzuvae dosage to 30 mg orally once daily in the evening for 14 days when used concomitantly with a strong CYP3A4 inhibitor. Avoid concomitant use with CYP3A4 inducers, as concomitant use may decrease the efficacy of Zurzuvae.

NEW DOSAGE FORMS

MELPHALAN
(Melphalan—Apotex)

Drug class: Melphalan is an alkylating drug.

Indication: Melphalan injection is indicated for palliative treatment of patients with multiple myeloma for whom oral therapy is not appropriate.

Recommended dosage and administration: The recommended dosage is 16 mg/m^2 administered intravenously over 15 to 20 minutes at 2-week intervals for four doses, then, after adequate recovery from toxicity, at 4-week intervals.

Common adverse effects: The most common adverse reactions are decreased neutrophil count, decreased white blood cell count, decreased lymphocyte count, decreased platelet count, diarrhea, nausea, fatigue, hypokalemia, anemia, and vomiting.

Boxed warning: Severe bone suppression with resulting infection of bleeding may occur. Controlled trials comparing I.V. melphalan to oral melphalan have shown more myelosuppression with the I.V. formulation. Monitor hematologic parameters. Hypersensitivity reactions, including anaphylaxis, have occurred in approximately 2% of patients who received the I.V. formulation of melphalan. Discontinue treatment with melphalan injection for serious hypersensitivity reactions. Melphalan produces chromosomal aberrations in vitro and in vivo. Melphalan injection should be considered potentially leukemogenic in humans.

Warnings and precautions: Melphalan injection is contraindicated in those with a history of severe hypersensitivity to melphalan. Nausea, vomiting, diarrhea, or oral mucositis may occur. Provide supportive care using antiemetic and antidiarrheal medications as needed. Melphalan can cause fetal harm. Advise patients of reproductive potential and those with partners of reproductive potential of the potential risk to a fetus and to use effective contraception. Melphalan may cause ovarian function suppression or testicular suppression. Advise patients not to breastfeed during treatment. Consider a dosage reduction in renal insufficiency.

NEW COMBINATIONS

NIRAPARIB AND ABIRATERONE ACETATE
(Akeega—Janssen Biotech)

Drug class: Akeega is a combination of niraparib, a poly (ADP-ribose) polymerase inhibitor, and abiraterone acetate, a CYP17 inhibitor.

Indication: Akeega is indicated with prednisone for the treatment of adult patients with deleterious or suspected deleterious BRCA-mutated metastatic castration-resistant prostate cancer. Select patients for therapy based on an FDA-approved test for Akeega.

Recommended dosage and administration: The recommended dosage for Akeega is 200 mg niraparib/1,000 mg abiraterone acetate orally once daily in combination with 10 mg prednisone daily until disease progression or unacceptable toxicity. Patients receiving Akeega should also receive a gonadotropin-releasing hormone analog concurrently or should have had bilateral orchiectomy. Take Akeega on an empty stomach. Do not eat food 2 hours before and 1 hour after taking Akeega.

Common adverse effects: The most common adverse reactions are decreased hemoglobin, decreased lymphocytes, decreased white blood cells, musculoskeletal pain, fatigue, decreased platelets, increased alkaline phosphatase, constipation, hypertension, nausea, decreased neutrophils, increased creatinine, increased potassium, decreased potassium, increased AST and ALT, edema, dyspnea, decreased appetite, vomiting, dizziness, COVID-19, headache, abdominal pain, hemorrhage, UTI, cough, insomnia, increased bilirubin, decreased weight, arrhythmia, fall, and pyrexia.

Warnings and precautions: Myelodysplastic syndrome and acute myeloid leukemia, including cases with fatal outcome, have been observed in patients treated with niraparib, a component of Akeega. Monitor patients for hematologic toxicity. Test complete blood counts weekly for the first month, every 2 weeks for the next 2 months, monthly for the remainder of the first year, then every other month, and as clinically indicated. Monitor patients for hypertension, hypokalemia, and fluid retention at least weekly for the first 2 months, then once a month. Closely monitor patients whose underlying medical conditions might be compromised by increases in BP, hypokalemia, or fluid retention. Monitor liver function and modify, interrupt, or discontinue treatment as recommended. Monitor for signs and symptoms of adrenocortical insufficiencies. Increased dosage of corticosteroids may be indicated, before, during, and after stressful situations. Monitor blood glucose in patients with diabetes and assess if antidiabetic agent dose modifications are required. Use of Akeega plus prednisone in combination with ^{223}Ra dichloride is not recommended. Posterior reversible encephalopathy syndrome has been observed in patients treated with niraparib. Discontinue Akeega if this occurs. Akeega can cause fetal harm. Advise patients to use effective contraception. Avoid coadministration with strong CYP3A4 inducers. Avoid coadministration with CYP2D6 substrates for which minimal changes in concentration may lead to serious toxicities. Avoid use of Akeega in moderate or severe hepatic impairment. ■

Soothe those eyes

Mary Warner

For those with dry, itchy, red, or irritated eyes, nonprescription eyedrops can provide fast and inexpensive, but short-term, relief. A typical pharmacy shelf may contain over 50 different products designed to soothe the eyes, so it's important to understand which will provide the most effective relief.

Dry eye relief

Eyedrops are specifically formulated to treat different symptoms, with discomfort associated with dry eye disease ranking as the most common condition for which nonprescription eyedrops are used. Dry eye disease is most often caused by wind, smoke, reduced tear production, or extended use of a computer screen. Recent data show that in the United States, dry eye disease may affect as many as 5 million people, especially those 50 years and older.

Drops formulated as artificial tears to treat dry eye disease contain preservatives, inorganic electrolytes to achieve tonicity and maintain pH, and water-soluble polymeric systems. All artificial tear eyedrops provide ocular lubrication, but buffering agents, preservatives, pH, and other formulation components vary among products. Common ingredients include carboxymethylcellulose sodium, povidone, hydroxypropyl methylcellulose, glycerin, propylene glycol, and mineral oil.

Formulations without preservatives are less likely than those with preservatives to irritate the ocular surface. However, patients should be aware that preservative-free products should be discarded immediately after being opened and used to avoid contamination and possible infection if used again.

Examples of artificial tears include Systane Lubricant Eye Drops, TheraTears, Visine Dry Eye Relief, and Refresh Relieva.

Red and itchy eye treatment

Eyedrops intended to "get the red out" contain a decongestant—usually tetrahydrozoline or naphazoline—to constrict the superficial blood vessels in the eye. They're intended to be used only on an as-needed and short-term basis, as longer-term use can worsen dry eye symptoms and cause rebound hyperemia when the effects wear off. Examples of eye drops intended to relieve red eyes include Lumify Redness Reliever, Visine Redness Relief, Clear Eyes Redness Relief, and Bausch & Lomb Maximum Redness Reliever.

Itchy eyes from allergies can be treated with eye drops that contain an antihistamine and a decongestant to reduce redness, irritation, and itchiness. These are most effective at controlling symptoms from pet dander, pollen, and dust and should be used only as needed. Examples of itchy eye relief products include Visine Allergy Relief, Clear Eyes Maximum Itchy Eye Relief, and Bausch & Lomb Alaway Allergy Eye Itch Relief.

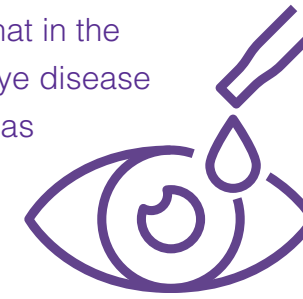
Eye washes can also be used to control itching and irritation from allergies; they also remove foreign particles, such as air pollutants and pollen, from the eyes. They contain primarily sterile water with a preservative to prevent contamination. Using an eye wash daily can sometimes alleviate the need for mediated eye drops. Examples of these products include Bausch & Lomb Eye Wash, Systane Eye Wash, and Optrex Eye Wash.

Safety concerns

Under the Federal Food, Drug, and Cosmetic Act, eye drops must be sterile to be safe for use. Unfortunately, however, this is not always the case, and several brands of OTC eye drops have been pulled from pharmacy shelves this year after they were found to contain drug-resistant bacteria.

In January 2023, FDA warned against using EzriCare Artificial Tears and Delsam Pharma's Artificial Tears because of possible contamination with *Pseudomonas aeruginosa*. Then in August 2023, FDA told consumers to immediately stop using Dr. Berne's MSM Drops 5% Solution and LightEyez MSM Eye Drops–Eye Repair due to possible bacterial contamination, fungal contamination, or both. Contaminants found in the products include Bacillus, *Pseudomonas, Mycobacterium, Mycolicibacterium,* and *Methylorubrum* bacterial species, as well as *Exophiala* fungal species.

Recent data show that in the United States, dry eye disease may affect as many as 5 million people, especially those 50 years and older.



These products also contain methylsulfonylmethane as an active ingredient, though it hasn't been approved for use in ophthalmic medications in the United States.

FDA warned that use of contaminated eye drops could result in minor to serious vision-threatening infections which could possibly progress to a life-threatening infection, and CDC said that anyone who used these products and has symptoms of an eye infection—including yellow, green, or clear discharge from the eye; redness of the eye or eyelid; increased sensitivity to light; and eye pain or discomfort—should see a doctor immediately.

What to tell your patients

Ensure that patients understand that while artificial tears can be used several times daily (most often in the morning and before bed), medicated eyedrops that contain a decongestant or antihistamine should be used only as needed. Most nonprescription eye drops are inexpensive and provide fast relief, but the relief is short-term, and patients with chronic problems should see their ophthalmologist to rule out more serious eye conditions. ■

The hydration boom: Sports and energy drinks

Mickie Cathers

Sports and energy drinks have exploded on the scene and now crowd the shelves with bright new brands and flavors. There are thousands of choices for the consumer in grocery stores, pharmacies, and online, all offering a host of benefits beyond simple hydration. But do we know what we're drinking?

The expanding popularity of caffeinated energy drinks, and the larger hydration category of supplements, is expected to continue growing by almost $70 billion from 2022 to 2027. According to The Vitamin Shoppe's Health & Wellness Trend Report 2023, the hydration category has seen an over 200% surge in website searches over the past year. Consumers are seeking branded, flavor-infused hydration products with added electrolytes. Industrywide, this category has seen massive growth as ready-to-drink combinations as well as in powders, tablets, and stick packs.

Traditionally, hydration products such as sports and energy drinks were associated with exceptionally active individuals such as athletes, but now sales data show it's new, younger consumers driving the sharp increase in hydration sales. The Vitamin Shoppe reported that about 25% of new customers ranged between 19 and 30 years old.

The booming business of energy drinks is supported by celebrities, professional and college athletes, and social media influencers, with some advertising targeted at those under 18 years.

Sales data show it's new, younger consumers driving the sharp increase in hydration sales.

"The rapid increase of marketing 'sports drinks' to younger athletes and targeting youth sports is highly concerning," said Ashley Anderson, RPh, MBA, clinical sports pharmacist. "Social media influencers with no medical training are promoting products that are questionable, despite their enormous popularity."

Energy drinks versus sports drinks

The line between sports and energy drinks has been blurred and for most, telling the difference between the two is difficult—especially when these drinks are stored on shelves next to one another.

"There is a difference between energy and sports drinks," said Jessica Beal-Stahl, PharmD, clinical sports

The danger of electrolyte imbalance

Our bodies need electrolytes—such as potassium, sodium, magnesium, and calcium—in order to maintain fluid balance, turn nutrients into energy, and support muscle control and heart rhythm. Sport drinks are sold with the promise of replenishing electrolytes, but an imbalance can lead to a whole host of issues.

- Too much sodium (hypernatremia) can cause dizziness, vomiting, and diarrhea.
- Too little sodium (hyponatremia) can cause nausea, vomiting, headache, and confusion.
- Too much potassium (hyperkalemia) can impact kidney function and cause heart arrhythmia, and nausea.
- Too much magnesium can cause muscle weakness, nausea, dizziness, confusion, and heart arrhythmia.

"Patients may be drinking a coconut water 'blend' that has a high potassium content, added BCAAs, and glucoranolactone, but may not be balanced to replace the actual losses of electrolytes from sweating and heavy breathing," said Ashley Anderson, RPh, MBA. "This type of unscientific formulation is potentially unsafe, raising a risk of hyponatremia or hyperkalemia. Many younger athletes are already at elevated risk of exercise-induced rhandomyolysis with intense training in the heat, or after a summer break and returning to intense training. This, combined with having less oversight from athlete support personnel (compared to amateur or elite athletes who receive more expert guidance), can lead to harmful effects." ■

pharmacist for The Athlete's Pharmacist and director of clinical services at Hobbs Pharmacy in Merritt Island, FL. "Energy drinks usually contain caffeine or other stimulants as ingredients. Sports drinks don't usually contain caffeine but offer carbohydrates and electrolytes intended to refuel athletes with sugar and electrolytes lost while training or competing."

Sports drinks

Popular sports drinks include Gatorade, Accelerade, Powerade, Nuun, VitaminWater, and Propel, among others. These are primarily used by athletes and those engaging in sports in which sweat and sodium is lost.

"Sports drinks were made to rehydrate and refuel," said Beal. "Athletes need both carbohydrates and electrolytes for training or competition for peak performance. Yet, many people use sports drinks as just regular hydration, which is not their intended purpose. When used outside of sports, they supply high amounts of simple sugars that can cause blood glucose spikes and crashes, yielding more fatigue."

Energy drinks

Popular energy drinks include Red Bull, Monster, Prime, Ghost, ZOA, Celsius, and Rockstar and can include ashwagandha, branched-chain amino acids (BCAAs), B vitamins, coconut water, electrolytes, L-theanine, and mushrooms. Per CDC, energy drinks typically include large amounts of caffeine, added sugars, other additives, and stimulants such as guarana, taurine, and L-carnitine.

"Athletes need both carbohydrates and electrolytes for training or competition for peak performance. Yet, many people use sports drinks as just regular hydration, which is not their intended purpose."

Despite providing boosts in energy, the stimulants in these drinks can have harmful effects on the nervous system and may increase BP, heart rate, and breathing. Adverse effects include dehydration, heart complications (e.g., irregular heartbeat or heart failure), anxiety, and insomnia.

These drinks are advertised as increasing and supporting focus, alertness, energy, and performance in exercise, workouts, and gaming or esports. Energy drinks are available in dozens of flavors, with the most popular being fruit flavors such as peach, sour pink lemonade, tropical punch, or sour gummy candies.

"Sports drinks may have a place for teen athletes, but not energy drinks," said Beal. "Many teens may take energy drinks to give them an 'edge' in sports, but the American Academy of Pediatrics warns that safe consumption levels of energy drinks have not been established for adolescents. The NCAA also has limits to the amount of caffeine an athlete can have in their system before [they are] considered to be at a banned level."

Caffeine levels

The American Academy of Pediatricians recommends children under the age of 12 years consume no caffeinated beverages. A general guideline for those over 12 years is a maximum of about 100 mg/day of caffeine. FDA regulates the amount of caffeine in sodas, but not in energy drinks. FDA also doesn't recognize a difference between energy and sports drinks, and they don't review labels of either to determine safety.

"Caffeine is the main 'energy' ingredient in energy drinks," said Beal. "Its ability to enhance performance, under certain conditions, has been well documented. Usually, 100–200 mg is an acceptable amount to improve alertness."

Some energy drinks contain massive amounts of caffeine, which can dramatically impact sleep quality and quantity, cause headaches, GI symptoms such as upset stomach or diarrhea, nervousness, increased anxiety, or heart palpitations. The energy drink popular with youth sports, Prime, lists 200 mg of caffeine per serving on the label, but also contains other stimulants. Plus, most consumers don't stop at one serving.

What to tell your patients

"Pharmacists, as a trusted source of information, can act now to dispel misinformation by starting conversations with patients, and colleagues, friends, and coaches," said Anderson.

Many patients may substitute these products for soda or water consumption without awareness of what ingredients are in sports and energy drinks or the impact the ingredients may have on their physical or mental health.

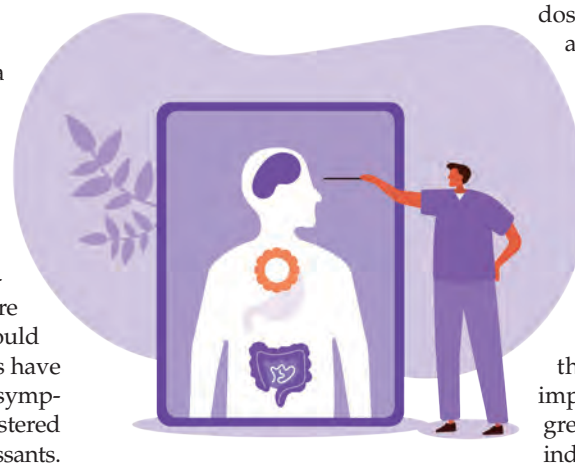
"Sometimes having that conversation with patients about what they are drinking and eating can help prevent adding medication," said Beal. "Often, I find that many don't realize the impact that the sugar of sports drinks has on their blood glucose, and thus nervous system and mood."

When asking patients about hydration and what they prefer to drink, be aware of sodium content and keep in mind that many medications influence thirst, urinary output, or loss of electrolytes, added Anderson. ■

Probiotics enhance antidepressant efficacy for major depressive disorder

Lauren Howell, PharmD

A study published in the August 2023 issue of *JAMA Psychiatry* suggests that probiotics could be used to bolster the response to antidepressant treatment in patients with major depressive disorder. The study found that individuals taking a daily probiotic for 8 weeks had a greater improvement in anxiety and depression symptoms than those taking a placebo.



It is a commonly accepted idea that targeting the microbiota–gut–brain axis is a promising pathway for new treatments for mood disorders, including major depressive disorder. With approximately 60% of individuals showing some degree of nonresponse to first-line treatments, there is a need for new options that could help fill this gap. Previous studies have found a reduction in depressive symptoms when probiotics are administered as adjunctive therapy to antidepressants. These studies, however, have lacked the ability to provide the safety and efficacy data that is needed for probiotics to be a widely used option in clinical practice.

The study by Nikolova and colleagues attempted to provide acceptability and tolerability data and estimates of intervention effect size for probiotics when used as adjunctive treatment for patients with major depressive disorder.

Study design

This study was a single-center, double-blind, placebo-controlled pilot randomized clinical trial. The participants consisted of 50 outpatients with a primary diagnosis of major depressive disorder and a Hamilton Depression Rating Scale (HAMD-17) score of greater than 13. The participants were all taking an antidepressant at a stable dose for at least 6 weeks and were not permitted to make any dosing changes during the study period.

Exclusion criteria included bipolar disorder, psychosis, eating disorders, personality disorders, substance dependence, suicidal ideation, serious medical illness, GI disease or surgery, use of antibiotics or probiotics in the past 12 weeks, current or regular use of GI medication, smoking, pregnancy, breastfeeding, and a vegan diet.

Participants were randomly assigned to either take four capsules of probiotic (2 x 10^9 colony-forming units per capsule) or four placebo capsules. The probiotic contained 14 strains of *Bacillus subtilis*, *Bifidobacterium bifidum*, *Bifidobacterium breve*, *Bifidobacterium infantis*, *Bifidobacterium longum*, *Lactobacillus acidophilus*, *Lactobacillus delbruecki subsp bulgaricus*, *Lactobacillus casei*, *Lactobacillus plantarum*, *Lactobacillus rhamnosus*, *Lactobacillus helveticus*, *Lactobacillus salivarius*, *Lactococcus lactis*, and *Streptococcus thermophilus*.

Participants attended visits at baseline, week 4, and week 8. The primary outcome was a change in depressive scores at week 8 based on the HAMD-17 score. Other outcomes included changes in anxiety, clinical status, and adherence. Information regarding adverse events and GI symptoms was also collected.

Results

Among the trial participants, baseline depression severity was moderate and 92% of the participants were taking an SSRI. Of the participants, 43% met the criteria for generalized anxiety disorder in addition to the major depressive disorder diagnosis. One difference noted between treatment groups was that all seven individuals who self-reported as Asian (non-Chinese) were randomized to the probiotic treatment group.

The researchers determined that adherence was high, with 97.2% of doses being taken as required based on a capsule count. No serious adverse reactions were reported during the study period and no participants withdrew from the study because of adverse effects. Nausea and indigestion were both reported as adverse reactions among the probiotic group, but these symptoms did not have to be treated with medication. The overall results of the study showed that depressive symptoms were improved in both study groups, but a greater reduction was seen among the individuals in the probiotic group from week 4.

Looking forward

This trial demonstrates the safety, acceptability, and therapeutic potential of probiotic therapy in patients with major depressive disorder. The treatment group showed greater improvement in depressive symptoms than the placebo group as seen in previous studies. With probiotics being a readily available and scalable intervention, this information suggests probiotics may be a new option for patients when used as adjunctive therapy to antidepressants.

Further research should be done to determine if the results of this study are replicable in patients being treated with other medication classes outside of SSRIs. Few studies have been performed to examine anxiety symptom response to probiotics and this area should continue to be explored as the findings of this study suggest that these symptoms may have been improved by the probiotic therapy. A larger-scale study with more participants should be conducted to continue to evaluate the efficacy of probiotics in major depressive disorder. ■

A sweetener in the limelight: Does aspartame cause cancer?

Clarissa Chan, PharmD

In July 2023, the American Cancer Society (ACS) revised its recommendations to align with WHO's International Agency for Research on Cancer (IARC) and other organizations to advocate for additional research on the potential association between aspartame ingestion and cancer risk.

Pharmacy Today spoke with Tyler Williams, CEO of ASI Food Safety in St. Ann, MO, and Darin Detwiler, PhD, a consumer food safety advocate and an associate professor at Northeastern University in Boston, to help pharmacists advise patients on aspartame dietary considerations.

What's the scoop?

Aspartame, a widely used artificial sweetener since the 1980s, has raised health concerns, notably related to its potential link to cancer—especially leukemias, lymphomas, and liver cancer. IARC has categorized aspartame as "possibly carcinogenic to humans," indicating limited evidence of its carcinogenicity.

Conversely, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) has concluded that the current evidence doesn't convincingly associate aspartame consumption with cancer, nor does it pose a health threat based on existing dietary exposure estimates.

Regulatory bodies like FDA and the European Food Safety Authority affirm the safety of aspartame for the general population when ingested within approved parameters and under current exposure levels. ACS also conducts independent studies to discover any potential associations between these substances and cancer.

How do dosage levels of aspartame correlate with cancer risk?

When declaring aspartame a carcinogen, IARC pointed to a French study from 2022, which found that individuals who consumed higher-than-average amounts of aspartame daily were at increased risk of developing breast cancer and/or obesity-related cancer, said Williams from ASI Food Safety, a food safety company for almost 100 years.

FDA, however, argues that just because aspartame is labeled by IARC as "possibly carcinogenic to humans," it does not necessarily mean that aspartame is linked to cancer.

When it comes to the sugar packets typically seen at restaurants and coffee shops, FDA claims it takes up to 75 packets of Equal (a common aspartame sweetener) in order to reach the acceptable daily intake (ADI).

"An adult weighing 132 lbs would have to drink between 12 and 36 cans of diet soda every day to be at risk, but this also depends on the amount or dose of aspartame in each beverage," said Williams. "A 12-ounce can of diet soda contains about 192 mg, or 0.007 ounces, but some may contain more, which is why it is so important to read the labels of what you are buying."

Is occasionally consuming large amounts of aspartame harmful?

Occasional large doses of aspartame should be avoided, especially if consumed beyond the 40 mg/kg of body weight per day that JECFA recently reaffirmed as its standby ADI, said Williams.

How closely regulated is aspartame?

"Nobody is paying attention to how much aspartame is really in their foods, and label regulations are not specific on listing amounts [of sweeteners] included," said Detwiler, referring to the many different sweetener formulations such as sucrose, fructose, etc.

Many direct-to-consumer energy drinks use social media influencers to advance their marketing. These market disruptors avoid some of the regulatory compliance checks and balance steps in the food supply system, he said.

How to avoid aspartame

For individuals who prefer to avoid aspartame, ACS advises individuals to check the ingredient labels of food and drink products first. Any product containing aspartame must include the warning "Phenylketonurics: Contains phenylalanine."

Monk fruit sugar is a plant-based, natural powder alternative to aspartame that doesn't include any additives, said Williams.

Is consuming aspartame better than sugar for weight loss?

Aspartame is about 200 times sweeter than table sugar and typically has zero calories, making it an appealing option for weight loss. But that doesn't mean it's better than regular sugar, said Williams.

In fact, WHO claims that sugar substitutes do not benefit long-term weight loss goals. While all types of sugar should be limited, natural sugars found in fruits should be preferred over artificial sweeteners.

"While there are gaps and changing information in research, the best statistics are set for a 150-lb healthy American male," said Detwiler. "The research indicates that he would have to drink nearly 20 cans of Diet Coke [per day] to be concerned." ■

First OTC oral contraceptive gains FDA approval, puts pharmacists in significant position

Loren Bonner

Pharmacists can add norgestrel (Opill–Perrigo), a progestin-only birth control pill, to the list of reproductive health care options offered to patients.

On July 13, 2023, FDA approved norgestrel, also known as a mini-pill or nonestrogen pill. The manufacturer expects it to be available on pharmacy shelves in early 2024.

"Data clearly demonstrate that women can safely and effectively use this product, and FDA acknowledged this in their unanimous decision to grant this product OTC status," said Rebecca Stone, PharmD, from the University of Georgia College of Pharmacy.

The daily oral contraceptive contains 75 µg of norgestrel.

Progestin only

In general, progestin-only pills work by thickening the cervical mucus—which inhibits the luteinizing hormone surge and thereby possibly prevents ovulation—and by causing atrophy of the endometrial lining, said Kassandra Bartelme, PharmD, from Concordia University Wisconsin School of Pharmacy.

According to Sally Rafie, PharmD, founder of Birth Control Pharmacist, progestin-only birth control pills are safer than the more commonly prescribed combined hormonal contraception and have almost no contraindications.

"Pharmacists should familiarize themselves with this new product, primarily with regard to efficacy and instructions for use," said Rafie, who testified in support of the manufacturer's application for OTC status at the FDA Advisory Committee hearing in May 2023. She was later told her testimony helped make the decision to recommend approval.

"The current guidance for progestin-only pills calls for them to be taken at the same time each day, within a 3-hour window," said Rafie.

However, Rafie said that data show that taking a progestin-only pill containing norgestrel 6 hours late or missing one pill entirely appears to have little impact on contraceptive efficacy, such as cervical mucus thickening.

Brushing up on contraceptive knowledge

Bartelme said pharmacists should learn from their store or district managers where Opill will be located in the store: on shelves or behind the pharmacy counter.

"Pharmacists will be patients' primary in-person resource for questions regarding the OTC birth control pill," she said.

Pharmacists can brush up on their contraceptive knowledge though continuing education programs specific to this topic, according to Stone. Pharmacists may encounter situations in which patients use oral emergency contraception and may not be able to refill their regular prescription contraceptive, using Opill as a bridge.

"This is an appropriate use of this product but may require more in-depth counseling regarding the logistics of how to do this effectively," said Stone. "I recommend referring to the U.S. Selected Practice Recommendations as a counseling resource."

The U.S. Selected Practice Recommendations for Contraceptive Use (2016) and the U.S. Medical Eligibility Criteria for Contraceptive Use are two key guideline documents that provide information for safe and effective use, she noted.

Brief counseling points

- Opill can be started at any time. If not started on the first day of the period, use condoms for the first 2 days.
- Take the pill within a 3-hour window each day.
- Patients may have irregular bleeding and/or spotting.
- Medical contraindications are rare but include a history of or current breast cancer, liver tumors, and severe cirrhosis.
- Do not take Opill with strong CYP3A4 inducers (e.g., some anticonvulsants, rifabutin, rifampin), as they degrade Opill and it may not work. Interacting drugs may include those taken for seizures, tuberculosis, HIV/AIDS, pulmonary hypertension, or supplements containing St. John's Wort.
- Patients should not take Opill if they are already using a hormonal contraceptive.
- Opill currently is not approved as an emergency contraceptive, nor does it protect against STIs. ■

Price and access

Patients will be able to obtain Opill with a prescription from their health care provider, including pharmacists in some states, or OTC, according to Rafie.

Provided that Opill is affordable, it would expand access. Opill's manufacturer has expressed its commitment to making the product affordable and accessible.

"The cost is expected to be around $20, but we will have to wait and see," said Rafie.

In some states, health plans will be required to cover the OTC birth control pill, and pharmacies will likely be involved in processing those claims.

Although the Affordable Care Act mandates that health insurance plans cover prescription contraception, that does not extend to OTC versions. Only a few states have laws requiring coverage for OTC birth control.

"We are still working on how to operationalize health plan coverage of the OTC pill. Pharmacists will continue to provide patient education on OTC and Rx birth control products," said Rafie.

A recent executive order by President Biden called on the federal government to soon take action to require insurance companies to cover OTC birth control. ■

ON THE COVER

Pharmacists fill needed health care gap for rural Americans

Loren Bonner

Rural Americans, who account for about one-fifth of the population, are generally older, have higher rates of obesity and diabetes, and tend to have worse health outcomes. Less access to health care only exacerbates poor health outcomes for many living in these parts of the country.

According to HHS, while 15% of the U.S. population lives in rural areas, less than 10% of physicians practice in these communities. An increasing number of health systems in rural areas are closing their doors, too, mostly because of problems with funding. But pharmacists who provide care to rural Americans are increasingly filling these needed gaps in care.

Studies show that 9 in 10 Americans live within 5 miles of a pharmacy, and patients with greater health needs visited their community pharmacy an average of 35 times per year compared to four visits to their primary care provider and nine visits to specialists.

Most pharmacists who practice in rural America, like Allison Reichert, PharmD, go the extra mile caring for their community. Many patients have Reichert's cell phone number, and her pharmacy offers an emergency after-hours line. While this may sound shocking, Reichert said it's actually rare to get a late-night call, since a rural setting means a smaller population. Plus, patients have a personal relationship with Reichert and respect her time.

Pharmacy Today profiled Reichert and two other pharmacists practicing in rural America to get a better understanding of the critical role they are playing in America's health care infrastructure.

Allison Reichert, PharmD, Illinois

Allison Reichert, PharmD, has been known to call a game of Bingo at the local senior center when she's there providing vaccines and quarterly BP readings.

"Most [of them are] our patients," said Reichert, vice president of operations for Bode Drugs in Vienna, IL. Reichert and her father, Carl Bode, RPh, own and operate two rural pharmacies in southern Illinois. One of their stores, located in Mound City, IL, has been in operation for over 100 years. "Spending time with our patients also gives us a chance to answer questions, gives us an opportunity to schedule [a medication therapy management session], and provides a space to be more accessible."

She makes vaccines more accessible, too. Reichert and her pharmacy team meet patients where they are—physically going out to locations ranging from assisted living facilities to local banks—and offering individuals a full range of vaccines. Not just flu vaccines—COVID-19, pneumonia, and shingles vaccines, too.

"In a rural community, other vaccines can go by the wayside, so we set up pneumonia clinics or shingles clinics, and when we go to them, we find we have more takers," said Reichert.

Allison Reichert, PharmD

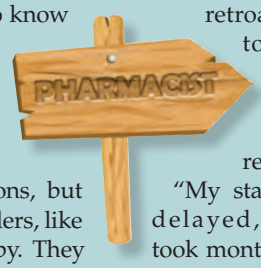
Reichert said being accessible is just part of providing care in a rural setting.

"In a rural area, a lot of patients don't have transportation. It might be 35 miles to the doctor, so that's something to keep in mind," said Reichert. "I do feel like we are used as that frontline health care provider," she said.

The main physician in town is across the parking lot from one of their pharmacies, and they work closely with that provider.

Bode Drugs offers compliance packing for assisted living facilities, but also

to people in the community. Most come recommended from the nearby physician. Reichert said compliance packaging is crucial in rural areas. "A patient's children may have moved away, so it's comforting for the kids to know their parents are being taken care of in that way."



Reichert points out that their pharmacies are also full-service retail pharmacies offering not only prescriptions, but OTC products. No large retailers, like Walmart or Target, are nearby. They also deliver medications daily to the corrections facility, which houses federal, state, and local prisoners.

Reichert's pharmacies have been designated by the State of Illinois as "critical access pharmacies," which according to the definition in the legislative language of the Illinois Public Aid Code, is an Illinois-based brick-and-mortar pharmacy that is located in a county with fewer than 50,000 residents and that owns fewer than 10 pharmacies.

The Critical Access Pharmacy program was developed to help provide retroactive monetary assistance to qualifying pharmacies for Medicaid prescriptions dispensed, which are significantly underreimbursed.

"My state payments were always delayed," said Reichert. "They took months. The critical access [designation] gets [us] guaranteed online payment in addition to a better dispensing fee."

Reichert said they still have to confront DIR fees and other challenges community pharmacists are faced with these days, but the critical access designation has been helpful.

According to Garth K. Reynolds, BSPharm, RPh, executive director of the Illinois Pharmacists Association, the State of Illinois added additional pharmacies in the rules: the pharmacy must be located in a county with fewer than 50,000 residents, or located in a county with 50,000 or more residents and in an area within Illinois that is designated as a medically underserved area by HHS's Health Resources and Services Administration.

"We wanted to ensure pharmacies in both rural and urban areas could obtain access to the funding," said Reynolds. "Each fiscal year, we have had $10 million allocated for the program. This fiscal year will be the first year that we are projected to utilize the entire allocated funds."

Every day, Reichert feels the impact she makes on her community. "Being a place for patients to simply access health care has been so rewarding," Reichert said.

Ernest "Tony" Holland, RPh, Alabama

Ernest "Tony" Holland, RPh, who has been a practicing pharmacist for almost 40 years, has worked in chain community pharmacy, academia, and in clinical practice at the U.S. Department of Veterans Affairs (VA) in rural Alabama.

Ernest "Tony" Holland, RPh

In the Veterans Health Administration (VHA) setting, he said he's been especially well received.

"You develop a relationship with your patients [and] they lean upon you before they go to their physician," Holland said. "They look to us to manage therapy and to monitor chronic conditions. We see them first and alert the nurse practitioner they are working with."

He has provided endless clinical services to veterans ranging from lipid therapy clinics to cholesterol screenings to managing patient's drug therapy.

According to the U.S. Government Accountability Office, about one-third of veterans enrolled in the VHA live in rural areas.

"The biggest barrier with this population is transportation," said Holland. "When they need [medication] refills, we have a program [in which] we can be the gap in their next appointment and provide mail service."

VHA's Office of Rural Health allocated approximately $245 million dollars for 35 separate initiatives, such as transportation for veterans to VA facilities. However, according to the U.S. Government Accountability Office, VHA's Office of Rural Health does not communicate all of its funding opportunities across VA programs. As a result, the U.S. Government Accountability Office said VHA may be missing chances to fund research at VA facilities serving rural veterans with unique access issues.

"I see pharmacists as key players in the health care infrastructure in this country," said Holland. "We are accessible, we have a relationship with the patient, and we can speak with them and their families or caregiver."

Helping with prevention, screening, and vaccination is part of that infrastructure, according to Holland.

"We are standing in the gap," said Holland. "Let's not forget about medication errors. We bridge all those gaps."

Holland grew up in a small town in rural Alabama, where his local pharmacist influenced his life in a major way.

"In that pharmacy, I saw someone who looked like me. [The pharmacist] knew everyone by name and he worked with you, your condition. He inspired me to become a pharmacist over 40 years ago," Holland said.

Throughout his career, Holland has received numerous professional awards, and was the first African American president of the Alabama Pharmacists Association, serving from 2001 to 2002.

Holland said these days, compliance issues with patients are the most challenging part of patient care. "So many patients have socioeconomic barriers that may slow them down. It's a daily challenge for us," he said.

"I see pharmacists as key players in the health care infrastructure in this country."

Holland said there's an opportunity for telehealth in rural America now more than ever. "We need to increase access and achieve better health outcomes for patients," said Holland.

He does provide telehealth services within the VHA and has found it to be successful.

According to study findings published in *JAMA Network Open* on August 14, 2023, states that adopted less-restrictive policies surrounding the use of telepharmacy had fewer pharmacy deserts in the following year.

"More states need to get on board," said Holland.

Holland has been nominated for a position on the State Board of Pharmacy in Alabama and said if elected, he would recommend favorable telehealth policies to the state government.

Nikki Bryant, PharmD, Georgia

In Preston, GA, Nikki Bryant's pharmacy serves a town of about 400 residents. The closest chain community pharmacy is over 30 miles away.

"Rural America gets neglected a lot because the populations are so low," said Bryant, PharmD. "It's hard to focus energy and resources on these areas, but it doesn't mean those lives are any less important."

In fact, Bryant cares for most of her friend's parents. Those friends have moved away since jobs are limited in the area. Bryant herself lived in other areas of Georgia, working in chain community pharmacy, long term care pharmacy, and hospital pharmacy before eventually making her way back home to Preston.

"Rural America gets neglected a lot because the populations are so low."

In 2014, she opened Adams Family Pharmacy in her dad's local grocery store. The pharmacy was the first in over 60 years in the town of Preston.

"I started delivering medications—no one was doing that at that time," said Bryant. Her pharmacy now delivers to 12 counties, and 85% of their pharmacy business is delivery. "We started compliance packaging before that was a thing, too," said Bryant.

In 2019, she opened another pharmacy in the adjacent county. One of the chain community pharmacies there closed, causing the other main pharmacy to take on too many patients, who often had to wait for their medications.

But perhaps Bryant's biggest undertaking has been the rural health clinic she opened up in Preston.

"I did foresee the need," said Bryant. "The doctor in Stewart County was getting older and was about to retire, so I knew there was going to be excessive need."

Bryant's rural health clinic is the first ever full-time clinic in Webster County history.

Bryant said communication is much more open between pharmacists and other rural health providers.

"Our nurse practitioner in the clinic is my number-one prescriber in our town," said Bryant. "We work very closely.

For instance, most insurance companies want patients [discharged from a hospital] to be seen within 7 days. When the patient is discharged, we notify the provider, and we follow up on the medication changes. We are very in tune with taking care of the patient, whereas in other pharmacies, that continuity of care may easily get lost."

Nikki Bryant, PharmD

Owning and operating a rural health clinic and two pharmacies is challenging, however.

In this pharmacy setting, providing patients with prescriptions, comprehensive medication reviews, immunizations, and recently Paxlovid for COVID-19, is not financially viable, unfortunately.

"Pharmacy reimbursement is hard," said Bryant. "Last year, we had to add a bakery and some other things just to make it work."

But if there's anyone who will make it work, it's Bryant. She knows how much she is valued by her patients.

"Any negativity from patients just doesn't happen," said Bryant. Instead, her patients regularly tell her they don't know what they would do without her. ■

Despite discounts, insulin prices remain high

Lauren Howell, PharmD

The results of a recently published study suggest that despite new discounts, insulin prices substantially increased from 2012 to 2015. The study also found that new insulin products coming to the market caused an increase in discounting practices and lowered the net price for payers.

The study that was published in *JAMA Health Forum* in June 2023 set out to describe trends in insulin prices from 2012 to 2019, and more specifically, how these prices changed when several new insulin products entered the market from 2015 to 2017.

With 25% of patients admitting that cost hinders them from accessing the insulin that they need, insulin pricing has received much attention from the media and congress over the last few years. Throughout a series of congressional investigations, manufacturers have maintained the stance that insulin prices are decreasing due to confidential, commercial discounts that are negotiated between pharmaceutical manufacturers and PBMs.

Previous studies have established that drug prices decreased after generic drugs were introduced, but little research has been done on how new nongeneric drug competition affects pricing.

Five new insulin products entered the market between 2015 and 2017. Long-acting insulins Toujeo, Tresiba, and Basaglar were all approved, while Fiasp was also brought to the fast-acting market. Additionally, Admelog was introduced as a fast-acting insulin during this time. For the purposes of the study, Admelog was categorized as a fast-acting biosimilar insulin. Basaglar and Admelog are not true biosimilars because at the time that Admelog was approved, insulin was not yet considered a biologic and therefore could not have biosimilar products. In 2020, this classification changed and allowed for the introduction of interchangeable biosimilar products to be brought to the market.

Study findings

The authors categorized insulin products into three groups: long-acting insulin analogues (insulin glargine, insulin detemir, and insulin degludec), short-acting insulin analogues (insulin lispro and insulin aspart), and human insulin products (Novolin and Humulin).

Data were collected from net sales and total units from SSR Health, Medicare Part B and Part D 5% claims, Medicare Part D prescriber user files, Medicare and Medicaid spending dashboards, and the 340B covered entity database. Net pricing for drugs was estimated as list price minus commercial discount and represented the price that Part D and private insurance plans would face after rebates.

List prices for long-acting insulin products increased at an annual rate of 12.3% from 2012 to 2019. The mean net price of these long-acting insulin products increased from 2012 to 2014 and then decreased until 2019. This change averaged out to a growth rate of 0.9% across the 2012 to 2019 study period. The decrease in net pricing that was seen after 2015 was identified as a result of a significant increase in commercial discounts, which increased from 22.7% to 64.8% across the study period.

The list prices for short-acting insulin products increased at an annual rate of 12.7%. From 2012 to 2017, the mean net price increased; then, from 2018 to 2019, it decreased. There was an annual net growth of 3.4% across the study period. Mean commercial discounts also increased from 37.9% in 2012 to 66.1% in 2019.

The mean list price and net price of human insulin products increased by an annual rate of 12.3% and 9.2%, respectively, over the study period. Mean commercial discounts increased from 54.9% to 63.1% during this period as well.

What does this mean?

Overall, the results of this study showed that insulin products are highly rebated and that the net prices for payers increased at a slower pace than list prices from 2012 to 2019. Before new drugs were introduced to the market, the increase in discounts was not able to offset the increases in list prices. During that time, before competition was introduced, growth in list prices was also reflected as growth in net prices. ■

Not many pharmacists provide OTC syringes

Loren Bonner

Most pharmacists fully recognize the clinical benefits of providing OTC syringes to people who use drugs, particularly in reducing transmission of HIV and hepatitis C. But according to research findings from *JAPhA* published July 8, 2023, pharmacists may communicate this understanding while at the same time actively creating barriers to access in their practice settings, such as unfairly interrogating patients about their need for syringes or requiring extra steps to sell them syringes.

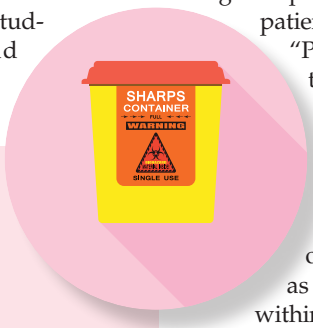
"If we're following the evidence—and the law—these actions don't make any sense," said lead author Jordan R. Covvey, PharmD, PhD, associate professor of pharmacy administration at Duquesne University School of Pharmacy.

Covvey and fellow researchers conducted a systematic review of 1,895 potentially relevant studies regarding OTC syringe sales among community pharmacy staff. A total of 36 studies spanning the last 25 years were ultimately included.

After analyzing the studies, researchers found relatively high support among respondents for harm reduction–related services within community pharmacies, but less common reports of staff engaging in said services themselves. When studies investigated the perceived positive or negative impacts of OTC syringe sales, prevention of bloodborne illness was widely understood as a benefit, while improper syringe disposal and safety of the pharmacy and its staff were commonly reported as concerns.

Stigmatizing attitudes and beliefs toward people who inject drugs were prevalent across studies, said researchers.

"One major takeaway that I hope pharmacists can use from this study is a better understanding of how stigma against people who use drugs harms patient care," said Covvey. "Pharmacy practice aims to take the best available evidence and translate it into clinical care. While traditionally this was focused on the use of medications, our roles have expanded over time into public health as well, given our accessibility within the community setting."



Harm-reduction services

The studies included in this systematic review described a variety of harm-reduction services and could serve as a starting point for pharmacists, including

1. Providing information on syringe disposal and safer injection drug use
2. Selling or freely providing sharps containers
3. Setting up a system for sharps disposal or needle exchange within the pharmacy
4. Providing brief interventions and/or referrals to SUD treatment when appropriate

Accessible health care

Effective tools, like sterile injection equipment, that reduce morbidity and

mortality from opioid misuse and abuse are greatly underused due to funding issues, politics, laws, misinformation, and stigma, according to Covvey.

"Pharmacists have this tool [sterile injection equipment] stocked in their pharmacies, which we know are one of the most accessible health care settings nationally," she said.

Covvey said pharmacists have the opportunity to provide tools for harm reduction as well as counseling, support, and connection with a health care professional.

"One major takeaway that I hope pharmacists can use from this study is a better understanding of how stigma against people who use drugs harms patient care."

"It's important that pharmacists personally interrogate the attitudes and beliefs that cause them discomfort [when] engaging with people who use drugs," Covvey said. "We don't need to generate more barriers for a population of patients already marginalized by health care and society, but rather [to] engage in evidence-based harm reduction whenever possible."

Limitations and strengths

Researchers were unable to provide pooled estimates of effect for any of the outcomes they assessed, mainly due to the variation in study designs and outcomes that were identified.

Also, they were not able to comment on cause-and-effects related to any of the attitudes, beliefs, and practices identified in the studies.

"Although the majority of the studies we assessed were quantitative in nature, what I think is a great strength of our analysis was our inclusion of qualitative studies as underlying context in the domains we assessed," said Covvey.

"These studies are where I think pharmacists can learn a lot about how OTC syringe sales really happen within practice. For me, reading quotes from interviews really helped me understand the different thought processes pharmacists have on this subject." ■

APhA's 2019 policy regarding harm reduction associated with injection use

1. APhA encourages state legislatures and boards of pharmacy to revise laws and regulations to support the patient-centered care of people who inject non-medically sanctioned psychotropic or psychoactive substances.
2. To reduce the consequences of stigma associated with injection drug use, APhA supports the expansion of interprofessional harm reduction education in the curriculum of schools and colleges of pharmacy, postgraduate training, and continuing professional development programs.
3. APhA encourages pharmacists to initiate, sustain, and integrate evidence-based harm reduction principles and programs into their practice to optimize the health of people who inject non-medically sanctioned psychotropic or psychoactive substances.
4. APhA supports pharmacists' roles to provide and promote consistent, unrestricted, and immediate access to evidence-based, mortality- and morbidity-reducing interventions to enhance the health of people who inject nonmedically sanctioned psychotropic or psychoactive substances and their communities, including sterile syringes, needles, and other safe injection equipment, syringe disposal, fentanyl test strips, immunizations, condoms, wound care supplies, pre- and post-exposure prophylaxis medications for human immunodeficiency virus (HIV), point-of-care for HIV and hepatitis C virus (HCV), opioid overdose reversal medications, and medications for opioid use disorder.
5. APhA urges pharmacists to refer people who inject non-medically sanctioned psychotropic or psychoactive substances to specialists in mental health, infectious diseases, and addiction treatment; to housing, vocational, harm reduction, and recovery support services; and to overdose prevention sites and syringe service programs.

FDA provides additional time for compliance with track-and-trace requirements

Mickie Cathers

On August 25, 2023, FDA announced a 1-year delay for supply chain trading partners to comply with the final enhanced drug distribution security requirements under the Drug Supply Chain Security Act (DSCSA), also known as track-and-trace, that were scheduled to take effect on November 27, 2023. FDA is calling this additional time a "stabilization period."

This delay affects the final implementation phase of a series of DSCSA requirements that have been unfolding since 2013.

The new compliance deadline of November 27, 2024, will help achieve DSCSA's prescription drug product traceability and security goals while minimizing supply disruptions and avoiding interruptions to patient care.

"This is a huge win for pharmacists who are still working toward complying with these final supply chain security requirements," said Michael D. Hogue, PharmD, FAPhA, FNAP, FFIP, executive vice president and CEO of APhA. "APhA has strongly advocated to FDA with our concerns for the readiness of all supply chain members, and we appreciate FDA taking this important step to delay compliance with these requirements to ensure patients will be able to get the medications they need without unnecessary disruptions in the supply chain."

This final step of enhanced drug distribution for the DSCSA requirements involves electronic verification, among other things.

What is a stabilization period?

The stabilization period is meant to allow trading partners, including dispensers (i.e., pharmacies) to implement, troubleshoot, and mature their electronic interoperable systems for exchanging transaction information, as required by law. The stabilization period is intended to avoid disruption to the supply chain and ensure continued patient access to drug products as the supply chain puts systems and processes in place.

FDA has specifically stated that this period isn't intended to provide, and shouldn't be viewed as providing, a justification for delaying efforts to comply with DSCSA. FDA is strongly urging trading partners to continue their effortrs to implement necessary measures to satisfy the new drug supply chain security requirements.

If a pharmacy hasn't already established how they will comply with the new requirements, they should start exploring their options with their wholesaler or vendors offering software solutions. It will take time to integrate these systems and set up processes for compliance and troubleshoot problems.

> ✔ Pharmacists who encounter products without a product identifier should determine whether the product is grandfathered. Dispensers may accept grandfathered product if there is documentation that the product was introduced into the drug supply chain before November 27, 2018. The full scope of the grandfathering exemption is described in the FDA final guidance titled Grandfathering Policy for Packages and Homogenous Cases of Product Without a Product Identifier. Read the guidance at apha.us/Grandfathered.

Latest updates

In new guidance, FDA provides information to assist supply chain partners, including dispensers such as pharmacies, in complying with the agency's requirements for enhanced drug distribution security for tracing at the package level.

In the final guidance, released September 2023, FDA details the use of electronic standards for tracing products through the pharmaceutical supply chain. FDA said it will allow trading partners to monitor drug

✔ If the dispenser, in coordination with the manufacturer, concludes that a product in the dispensers' possession or control is illegitimate, the dispenser shall follow specific steps outlined in DSCSA:

- Arrange for disposition of illegitimate product and assist with the trading partner's disposition.
- Retain a sample of the product for further physical examination or laboratory analysis.
- Notify FDA and all immediate trading partners within 24 hours of making an illegitimate product determination.
- Respond to notification from FDA that product is illegitimate and identify all illegitimate product subject to the notification.
- Terminate the notification if such a determination is made in consultation with FDA.
- Maintain records of disposition of an illegitimate product for 6 years after disposition.

products through the pharmaceutical supply chain using email exchanges and portals. The aim is to address the needs of smaller pharmacies, which may lack the encrypted internet connections necessary for exchanging Electronic Product Code Information Services (EPCIS) data. The guidance advises trading partners to use GS1's EPCIS standard to transmit information through the supply chain.

FDA said that this guidance finalizes the policy articulated in the July 2022 revised draft guidance to reflect the enhanced drug distribution security requirements in the law, including that only electronic methods of product tracing will be permitted and verification of product at the package level will be required, unless a waiver, exception, or exemption applies.

Current dispenser requirements

The Pharmaceutical Distribution Security Alliance, a coalition of supply chain partners of which APhA is an observer, recently published DSCSA questions and answers for dispensers. They note that dispensers' current track-and-trace obligations—those for which dispensers must already have systems and processes in place—are that

- They should only accept ownership of a product if the previous owner provides transaction history, transaction information, and a transaction statement (known as "the 3Ts").

✔ **Transaction information:** A paper or electronic statement that includes product name, strength, dosage form, National Drug Code (a unique, three-segment number that serves as a universal product identifier for drugs), container size, strength and dosage form, number of containers, transaction date, shipment date, name and address of the seller and buyer, and lot number.

✔ **Transaction history:** A paper or electronic statement that includes the transaction information for each prior transaction of the product back to the manufacturer.

✔ **Transaction statement:** A paper or electronic confirmation transferring ownership of the product.

- They must provide subsequent owners of a product with the 3Ts at the time of or prior to the transaction.
- They must capture and store the 3Ts, including lot level information if provided, for no less than 6 years after the transaction.
- They must reply to FDA or other federal or state agency requests for information within 2 business days.
- They must only engage in transactions with authorized trading partners, and
- They must conduct a suspect-product investigation that includes the capability to quarantine suspect products in their possession or control.

✔ Dispensers who transfer products to another dispenser without a specific patient need may need to register as a wholesale distributor or refrain from the transaction unless another exemption is satisfied.

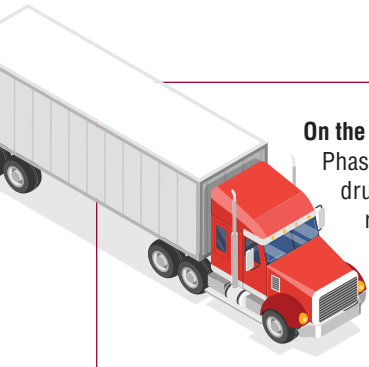
LEGEND

✔ Complete at least once
✔ Continuous requirement
✔ Key tip

What has already taken place

DSCSA, passed in 2013, created a stepwise approach for implementing requirements for supply chain security. The goal was to create an electronic, interoperable exchange of information that identifies and traces certain prescription drugs down to the package level as they move through the supply chain to protect consumers from counterfeit, stolen, contaminated, or otherwise harmful drugs. DSCSA requires pharmacies—referred to as "dispensers"—to use an electronic, interoperable system that tracks a drug at the unit level throughout the supply chain until it reaches the patient.

Requirements unfolded in several phases over this 10-year period, with the final requirements set to go into effect this November 2023. Certain benchmarks were to be hit in 2020.



On the horizon

Phase 3 of DSCSA's full implementation involves enhanced drug distribution security. Its compliance deadline has been recently updated to November 27, 2024.

Why it matters: an electronic system will improve FDA's ability to recall products, detect illegitimate products earlier, and secure the supply chain. The systems and processes that pharmacies must implement will change workflow as products are received and returned, among other circumstances.

- ✔ Exchange transaction information (e.g., product identifier at the package level) and transaction statements in a secure, interoperable, electronic manner.
- ✔ Implement systems or processes for package-level product verification, which may include use of aggregation and inference, as necessary.
- ✔ Implement systems or processes for verification of product at the package level, including the standardized numerical identifier.
- ✔ Implement systems or processes to promptly facilitate gathering the information necessary to produce the transaction information and transaction statement for each transaction going back to the manufacturer, if FDA or an authorized trading partner requests a suspect or illegitimate product investigation.
- ✔ If a dispenser enters into a written agreement with a third party—including an authorized wholesale distributor—to confidentially maintain required information and statements, the dispenser must maintain a copy of the written agreement.

Starting January 1, 2015, pharmacies can only do business with licensed wholesalers and pharmacies, and FDA-registered manufacturers.

As of November 27, 2020, pharmacies were required to buy and sell—what the track-and-trace law refers to as "engaging in transactions"—only products with a required "product identifier" on their packages.

Most products—although not all—packaged by manufacturers after November 27, 2018, are required to be affixed or imprinted with a product identifier that features the products' National Drug Code plus a unique serial number, lot number, and an expiration date. By November 27, 2020, dispensers should have put processes in place to ensure the product identifier is on the package when they received products that required it. The product identifier is included in both human-readable format and on a machine-readable data carrier in a 2D data matrix barcode.

"The challenge for dispensers is that not all drug product packages are required to have a product identifier, and there is no central database to check if a product should have one," said Ilisa Bernstein, PharmD, JD, FAPhA, senior vice president of pharmacy practice and government affairs at APhA. "If unsure, check with the manufacturer to see if a product identifier should be on the package."

There could be disruptions up and down the supply chain, leading to shortages or lack of access and availability of drugs for our patients.

Since January 2015, dispensers must have systems and processes for actions that must be taken if they have suspect or illegitimate product. It is important that dispensers have SOPs and train staff on the steps to take if they find suspect or illegitimate product, including the proper documentation and who to notify. FDA is enforcing this requirement and recently issued a warning letter to a firm that did not comply. "For suspect and illegitimate product, dispensers must still quarantine product, conduct investigations, and [arrange for] disposition [of] illegitimate product," Bernstein said.

Small business dispensers

DSCSA requires FDA to assess the impact of these requirements on small dispensers—those with 25 or fewer full-time employees—in order to ensure that the requirements do not impose undue economic hardship. If so, FDA is to determine timelines for compliance or alternative ways for small business dispensers to comply. FDA acknowledged that they received a number of letters from small business dispensers requesting a delay in compliance. Recently, FDA asked the public for comment on questions that will be posed to assess the impact. FDA is expected to start this study in the coming months.

APhA, the National Community Pharmacists Association, and other pharmacy partners collaborated to identify the economic impact of compliance on small business dispensers. They also had several meetings with FDA since DSCSA was passed and submitted letters informing them of the lack of readiness throughout the supply chain. APhA noted that without stable connections to trading partners and appropriate systems and processes, there could be disruptions up and down the supply chain, leading to shortages or lack of access and availability of drugs for our patients.

Going forward

FDA is strongly urging all members of the supply chain to continue their efforts to implement necessary measures to satisfy these enhanced drug distribution security requirements despite this 1-year delay. ■

Diagnostics, ears and eyes, family planning, and first aid

Nonprescription products offer preparations to treat a wide range of disorders. There is an expanding variety of home testing and monitoring kits available for patients interested in preventative care, detecting the presence or absence of a medical or physiologic condition, and monitoring therapy or results of a wellness routine. Pharmacists are in a prime position to offer self-care recommendations for patients seeking OTC relief.

Diagnostics

Blood glucose monitors

OneTouch....1
FreeStyle....2
Accu-Check....3

Blood pressure monitors

Omron....1

Nontouch digital thermometer

Braun....1
Vicks....2

Ears and eyes

Adult earache relief

Similasan....1
Debrox....2
Hyland's Naturals....2

Contact lens solution

Bausch + Lomb....1
OPTI-FREE Puremoist....2

Eye drops for pink eye

Similasan....1
Visine....2

Eye vitamin

PreserVision....1
Ocuvite....2

Multisymptom eye drops

Visine....1
Systane....2

Family planning

Condom

Trojan....1

Pregnancy test

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

First aid

Bandages

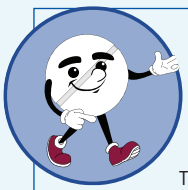
Band-Aid....1

Burn treatment and relief

Neosporin....1

Sunburn relief

Solarcaine....1
Banana Boat....2



Self-care survey redux

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

The current survey was conducted by BrandSpark/Newsweek International using scientifically valid methodology, and lists those nonprescription products most often recommended by pharmacists in the United States to consumers.

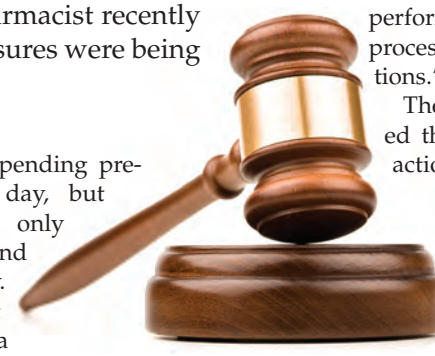
The winners were selected based on a survey of 1,716 pharmacists practicing in the United States who gave their unaided write-in opinions on which brands they'd recommend to patients in 86 categories. The highest share of citations as most trusted in the category determined the winner. If the margin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

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

Quantitative measures of pharmacist productivity

David B. Brushwood, BSPharm, JD

It is challenging to objectively evaluate the efficiency of health professionals. A designated task related to the provision of health care products or services may require a lengthy period of time to complete, or it may be accomplished very quickly, depending on the patient's condition, the nature of the product or service, and the environment in which the activity is being performed. Nevertheless, establishing productivity metrics for the performance of professional responsibilities in health care has become standard. A pharmacist recently challenged the manner in which quantitative measures were being used in the evaluation of his productivity.



Background

The pharmacist was working in a clinical role when the health care system issued a mandate to increase efficiency in pharmacy operations. Some clinic pharmacies were closed, and the pharmacist was reassigned to a role that primarily involved the review and resolution of pending prescriptions. Within that new role, the pharmacist criticized inefficiencies related to delays in patients receiving medications, the destruction of thousands of dollars' worth of prescription medications, and the extensive resources used to handle returned medications. An investigation was conducted, and the pharmacist's concerns were substantiated. Changes were made to reflect the findings of the investigation.

The pharmacist repeatedly failed to meet the performance standard for pending prescription processing. In 2018, successful performance required processing 125 pending prescriptions per day, but the pharmacist processed an average of only 76 pending prescriptions per day. In 2019 and 2020, successful performance required processing 120 pending prescriptions per day, but the pharmacist only processed 100 and 104, respectively. The pharmacist was placed on a Performance Improvement Plan (PIP), with which he refused to cooperate. The pharmacist filed an internal complaint alleging whistleblower reprisal, based on "numerous adverse personnel actions." An administrative judge (AJ) held a 5-day hearing to review the complaint. The judge denied the pharmacist's request for corrective action, and from this denial the pharmacist appealed to a United States Court of Appeals.

Quantitative measures of productivity are intended to avoid what has at times been referred to as "the tyranny of subjectivity."

Rationale

The appellate court reviewed the pharmacist's allegation that the AJ had "failed to consider scheduling inequalities, relied on unreliable metrics, and failed to find a hostile workplace."

The court first noted that there was "substantial evidence to conclude that there were no scheduling disparities between [the pharmacist] and other outpatient pharmacists." The court said that the AJ had "carefully compared [the pharmacist's] shifts to those of other pharmacists and found that those who worked the same or fewer number of pending shifts nonetheless filled more prescriptions than him."

The court also noted "clear and convincing evidence that similarly situated individuals who were not whistleblowers were also placed on a PIP, when they failed to meet the performance standard for processing pending prescriptions."

The appeals court affirmed the denial of corrective action.

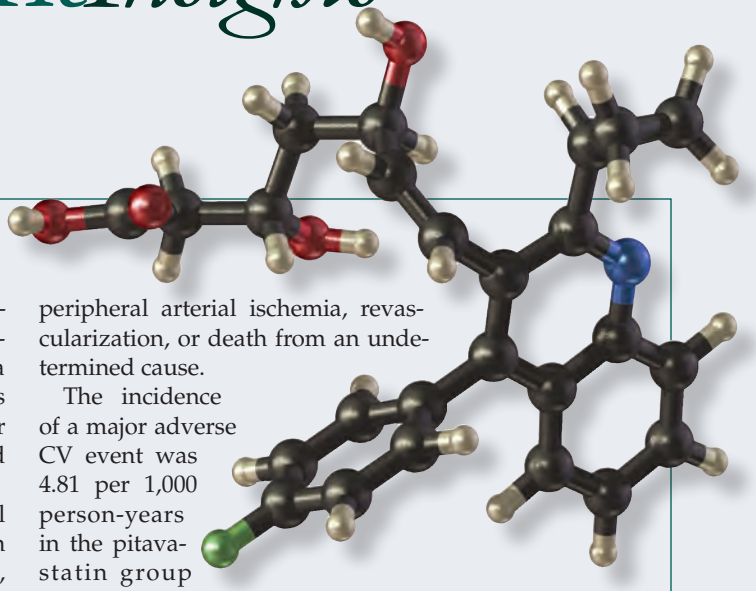
Takeaways

Negative performance evaluations can be annoying and insulting, particularly when they seem to be unfairly based on invalid criteria. On the other hand, it is important to appreciate how the commercial side of health care must be conducted efficiently. Cost constraints are genuine. Performance expectations are equally authentic. Health care is both a public service and a business.

Quantitative measures of productivity are intended to avoid what has at times been referred to as "the tyranny of subjectivity." A person who is evaluated as being "too slow" may wonder what criteria for production are being applied. If a specific number can be used as a criterion for productivity, then at least there is a possibility to understand the expectation and to appreciate how an evaluation is being made.

The foundational problem illustrated by this case is that sometimes clinical pharmacy services are viewed as being gratuitous luxuries that can be discontinued to promote efficiency. The necessity of clinical pharmacy care can be difficult to economically substantiate. A pharmacist who is transferred from a clinical role to a distributive role might have difficulty understanding the efficiency of such a move. ■

Inpatient*Insights*



Pitavastatin shown to prevent CVD in patients with HIV

Patients with HIV infections have twice the risk of developing atherosclerotic CVD compared with others, making prevention strategies for this population critical. According to a new study published in *NEJM* on August 24, 2023, patients with HIV infections who received pitavastatin had a lower risk of a major adverse CV event than those who received placebo over a median follow-up of 5.1 years.

The REPRIEVE investigators conducted a Phase 3 trial in which almost 8,000 participants from research sites in the United States, Canada, Thailand, South Africa, Brazil, Peru, Haiti, Zimbabwe, Botswana, Uganda, and India were randomly assigned to receive 4 mg of pitavastatin calcium daily or a placebo. All patients had HIV infection with a low to moderate risk of CVD and were receiving antiretroviral therapy. The primary outcome was the occurrence of a major adverse CV event, which was defined as a composite of CV death, myocardial infarction, hospitalization for unstable angina, stroke, transient ischemic attack, peripheral arterial ischemia, revascularization, or death from an undetermined cause.

The incidence of a major adverse CV event was 4.81 per 1,000 person-years in the pitavastatin group and 7.32 per 1,000 person-years in the placebo group, with muscle-related symptoms occurring in 2.3% of patients in the pitavastatin group and 1.4% of patients in the placebo group. The authors noted that other statins may have similar protective effects and that other strategies to lower LDL cholesterol may be useful in this population and should be compared with statin therapy with respect to efficacy, safety, and cost. ■

Can SGLT-2 inhibitors prevent gout flares?

SGLT-2 inhibitors are FDA-approved for managing adult patients with T2D to improve blood glucose control as an adjunct to diet and exercise. Because they are also known to decrease serum urate levels, it has been suggested that SGLT-2 inhibitors may also be useful in preventing recurrent flares of gout. Researchers from Massachusetts General Hospital and colleagues compared the number of gout flares and CV events among patients with gout taking SGLT-2 inhibitors versus patients taking DPP-4 inhibitors, another glucose-lowering medication not associated with serum urate levels or CV risk.

The study, a propensity score–matched, new-user cohort study, involved data from a general population database of patients with gout and T2D from January 1, 2014, to June 30, 2022. The primary outcome was recurrent gout flare counts from emergency department (ED), hospitalization, outpatient, and medication dispensing records. Secondary outcomes included myocardial infarction and stroke.

Results of the study, published in the August 2023 issue of *Annals of Internal Medicine*, showed that the flare rate was lower among patients who received SGLT-2 inhibitors than among those who received DPP-4 inhibitors (52.4 and 79.7 events per 1,000 person-years, respectively). Patients who received SGLT-2 inhibitors also had significantly fewer ED visits or hospitalizations and fewer myocardial infarctions. The question remains as to whether the same benefits would be seen in patients with gout but without T2D. ■

Coadministered pneumococcal conjugate vaccine may decrease immune response to hepatitis A vaccine

Hepatitis A vaccine (HepA) and pneumococcal conjugate vaccine (PCV) are increasingly used for pre-travel immunizations. Simultaneous administration of several vaccines prior to travel is a well-established practice, and providing 13-valent PCV (PCV13) together with HepA at pre-travel visits would be practical but data on coadministration of these two vaccines among adults have been lacking. A recent study in *Clinical Microbiology and Infection*, published on August 10, 2023, evaluated the safety and immunogenicity of coadministered PCV13 and HepA among over 300 adult volunteers at travel clinics at Helsinki University Hospital and Mälar Hospital in Eskilstuna, Sweden.

Patients were randomized into three groups receiving either PCV13, HepA only, or both. Antipneumococcal IgG concentrations, opsonophagocytic activity (OPA) titers, and total hepatitis A antibody concentrations were measured before vaccination and 28 ± 3 days after vaccination.

After vaccination, the mean concentration of hepatitis A antibodies was significantly lower in the PCV13 + HepA group than in the HepA group, with 83.5% of patients in the PCV13 + HepA group reaching a level of antibodies considered protective versus 96.2% of the patients in the HepA-only group. Increases in antipneumococcal IgG and OPA levels were comparable in the PCV13 + HepA and PCV13 groups, apart from a larger increase for serotype 3 in patients in the PCV13 + HepA group.

The authors concluded that while coadministration of HepA and PCV13 did not cause safety concerns or impact the patients' response to PCV13, apart from serotype 3, it did significantly impair antibody responses to HepA. Thus, coadministration of the first HepA dose and PCV13 may not provide sufficient protection against hepatitis A for travelers. Ensuring early single-dose protection against hepatitis A may require that travelers opting for both HepA and PCV immunization not be given the vaccines together. ■

Naloxone requirements of patients with novel potent opioid overdose

Novel potent opioids (NPOs) such as brorphine, isotonitazene, metonitazene, and N-piperidinyl etonitazene are increasingly being detected in patients with illicit opioid overdose in the emergency department (ED), but the naloxone requirements and clinical needs of patients with NPO overdose are unclear. According to a recent study published in *JAMA Network Open* on August 29, 2023, in-hospital naloxone dosing was higher for patients who tested positive for NPOs than for patients who tested positive for fentanyl alone.

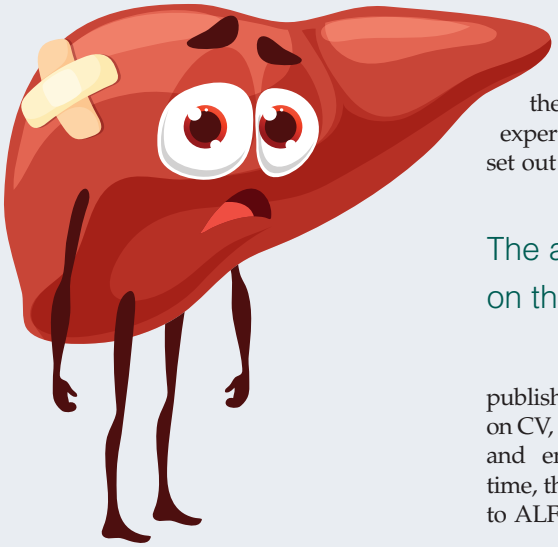
The authors conducted a subgroup analysis of data from the ongoing nationwide ToxIC Fentalog cohort study from 2020 to 2022 involving adults admitted to the ED who tested positive for NPOs. Patients were included in the analysis if their confirmatory testing was positive for an NPO analyte, including brorphine, isotonitazene, metonitazene, and/or N-piperidinyl etonitazene. The primary outcome was the total number of naloxone doses and total cumulative naloxone doses administered as part of routine clinical care following the overdose. Naloxone requirements and clinical sequelae of NPO-positive patients were compared with those testing positive for fentanyl only.

Findings of the analysis indicated that patients who tested positive for an NPO received a statistically significantly higher number of naloxone boluses in-hospital compared with patients who tested positive for fentanyl only. Patients who experienced metonitazene overdose were also more likely to suffer cardiac arrest and require cardiopulmonary resuscitation. The authors concluded that further study is warranted to confirm these preliminary results. ■

SCCM releases new guidance for patients with liver failure in ICU

Corey Diamond, PharmD

The Society of Critical Care Medicine (SCCM) has recently released the second part of their guidance on the management of acute liver failure (ALF) and acute-on-chronic liver failure (ACLF) in the ICU.



Published in the May 2023 issue of *Critical Care Medicine*, the guideline—compiled by 27 experts—continues SCCM's mission set out earlier in 2022. Their previously published recommendations focused on CV, hematological, pulmonary, renal, and endocrine/nutrition issues. This time, their guidance focuses on updates to ALF considerations in the setting of neurology, peri-transplant medicine, infectious disease, and gastroenterology.

Guideline structure

Part 2 of the SCCM's guidance of ALF and ACLF segregates recommendations into four distinct subgroups: Neurology, peri-transplant, infectious diseases, and gastroenterology.

The authors present 28 recommendations on the management of ALF and ACLF in the ICU. Overall, they include 5 strong recommendations, 21 conditional recommendations, and 5 recommendations with insufficient evidence.

The authors present 28 recommendations on the management of ALF and ACLF in the ICU.

Below is a summary of the panel's strong or conditional recommendations—those that have an evidence level of low or higher—that are pertinent to pharmacology. ■

Table 1. Strong recommendations

Subgroup	Recommendations	Rationale	Evidence level
Infectious disease	SCCM recommends using antibiotic prophylaxis in critically ill patients with ACLF and any type of upper GI bleeding. Typically, third generation cephalosporins.	Evidence suggests that upper GI bleeding in ACLF may predispose patients to bacterial infections. Prophylactic antibiotics may improve infection rate, rebleeding, and survival.	Moderate
Infectious disease	SCCM recommends using albumin in critically ill patients with ACLF and SBP. SCCM recommends albumin 25% 1.5 g/kg at SBP diagnosis and regardless of serum albumin levels and volume resuscitation status.	SBP may predispose critically ill patients with ACLF to shock, acute kidney injury, and organ failure. Evidence suggests albumin may reduce odds of mortality and renal impairment.	Moderate
Infectious disease	SCCM recommends broad-spectrum antibiotics for initial management of SBP in critically ill patients with ACLF. SCCM recommends limiting the use of third-generation cephalosporin as the initial empirical treatment to low-risk community-acquired patients with SBP.	Evidence suggests a trend of increased gram-positive and MDR pathogens in multiple geographic areas. Patients with advanced liver disease are at increased risk of MDR SBP.	Low
Gastroenterology	SCCM recommends using PPIs in critically ill patients with ACLF and portal hypertensive bleeding.	PPI may reduce rates of rebleeding and need for endoscopic intervention in patients with ACLF and portal hypertensive bleeding. Meta-analyses have found PPIs may not have impact on mortality in this population.	Low
Gastroenterology	SCCM recommends using octreotide or SSA for the treatment of portal hypertensive bleeding in critically ill patients with ACLF.	Evidence suggests SSAs are associated with 30 fewer deaths per 1,000 patients in this patient population.	Moderate

Abbreviations: ACLF, acute-on-chronic liver failure; MDR, multidrug resistant; PPIs, proton pump inhibitors; SBP, spontaneous bacterial peritonitis; SCCM, Society of Critical Care Medicine; SSA, somatostatin analog.

Table 2. Conditional recommendations

Subgroup	Recommendations	Rationale	Evidence level
Neurology	SCCM recommends using hypertonic saline in critically ill patients with ALF who are at risk for intracranial hypertension. Use 3% saline to raise sodium level between 145–155 mmol/L.	RCT by Murphy and colleagues suggests hypertonic saline reduces rates of intracranial hypertension but may not have impact on mortality. Risk factors of intracranial hypertension include hyperammonemia (>150 µmol/L), high-grade HE or evidence of multiple organ failure.	Low
Neurology	SCCM recommends lactulose in critically ill patients with ACLF and overt HE.	Evidence suggests lactulose may reduce HE, liver failure, variceal bleeding, infectious SBP and hepatorenal syndrome in this patient population. Lactulose may also have a mortality benefit in patients with overt HE.	Low
Neurology	SCCM recommends using PEG as an alternative to lactulose in critically ill patients with ACLF and overt HE. Use 4 liters of PEG enterally over 4 hours. However, there may be a concern for aspiration in advanced grades of encephalopathy and should be used cautiously.	A single center RCT demonstrated 4 liters of PEG over 4 hours led to faster resolution of HE.	Low
Neurology	SCCM recommends using rifaximin as adjunctive therapy in critically ill patients with ACLF and overt HE. Use rifaximin 550 mg BID.	Evidence suggests that patients with severe HE who receive rifaximin, in addition to lactulose, may have better symptom reversal and improved mortality.	Low
Infectious disease	SCCM recommends using antibiotics within 1 hour of shock onset in critically ill patients with ACLF, SBP, and septic shock.	Although there are no RCTs to guide this recommendation, observational data of small retrospective cohort studies suggest there may be higher mortality for each hour of delay after shock recognition in this patient population.	Low
Peri-transplant	SCCM recommends using a balanced (or normochloremic) crystalloid solution over normal (hyperchloremic) saline for peri-transplant fluid replacement in liver transplant recipients.	There is no direct evidence for this recommendation for liver transplant patients. However, indirect evidence of ICU and surgical patients suggests a mortality benefit when using balanced crystalloid solutions for fluid management.	Low
Peri-transplant	SCCM recommends using albumin over crystalloid for intraoperative volume replacement during liver transplant. Starches should not be used due to risk of coagulopathy and renal failure.	There is no direct evidence for this recommendation. Indirect evidence from patients with traumatic injuries, patients undergoing surgery, and critically ill patients suggests a mortality benefit.	Low

Abbreviations: ACLF, acute-on-chronic liver failure; ALF, acute liver failure; HE, hepatic encephalopathy; PEG, polyethylene glycol; RCT, randomized controlled trials; SBP, spontaneous bacterial peritonitis; SCCM, Society of Critical Care Medicine.

Study reaffirms detrimental effects of aggressive BP treatment in hospitalized patients

Olivia C. Welter, PharmD

Despite a body of continually growing evidence against the practice of aggressive BP treatment in hospitalized patients, some health systems still take an intensive approach to managing inpatient BP.

A study published in *JAMA* on May 30, 2023, adds further confirmation that this practice leads to greater risk of patients experiencing adverse drug events, which could lead to acute kidney injury, elevation of B-type natriuretic peptide or troponin, and transfer to an ICU.

Study background and findings

The study by Anderson and colleagues was conducted within the Veterans Health Administration and focused on older inpatient veterans. Because of this, the gender demographics are not balanced, with women accounting for only 2.6% of the over 66,000 patients included in the study. Patients could be included for review if they were over the age of 65 years, hospitalized for a non-CV diagnosis, and experienced elevated BP within their first 48 hours of hospitalization. The researchers defined intensive BP treatment as receipt of either I.V. or oral antihypertensives in the hospital that the patient had not taken prior to their hospital admission.

Researchers retrospectively evaluated patient data for individuals hospitalized between October 1, 2015, and December 31, 2017, and analyzed the data between October 2021 and January 2023. The primary composite outcome included mortality, ICU transfer, stroke, acute kidney injury, B-type natriuretic peptide elevation, and troponin elevation.

Overall, the study found that patients who received intensive BP treatment were more likely to experience one of the components of the primary composite outcome, with the exception of stroke and mortality. Patients who specifically received I.V. antihypertensives were the most at risk for experiencing any adverse event included in the primary composite outcome.

Other evidence

Over the years, several studies have been published which concluded that treating asymptomatic high BP in the hospital for noncardiac patients can increase risk of negative outcomes.

Ghazi and colleagues measured incidence of mean arterial pressure drop to ≥30% in hospitalized patients with aggressively treated BP, which can indicate potential harm. Their findings, published in the March 2022 issue of the *Journal of Clinical Hypertension*, found that I.V. antihypertensives were significantly more likely to cause this outcome than oral antihypertensives.

Additionally, a study published December 28, 2020, in *JAMA Internal Medicine* by Rastogi and colleagues found that when hospitalized patients had their hypertensive episodes treated during their admission and were discharged with intensified BP regimens, they were more likely to experience acute kidney or myocardial injury than untreated patients were. This was in addition to treated patients not having improved BP control a year after their hospitalization.

What's next?

Authors of the *JAMA* study suggested that a randomized clinical trial of inpatient BP treatment targets is needed, since most research conducted on rigorous BP management in a hospital setting is studied through retrospective data. While this type of data can still provide valuable insights into treatment practices, there isn't much control over variables. Randomizing patients for a study such as this is unlikely, however, due to the potential risks that come with randomizing patients to treatment in this setting.

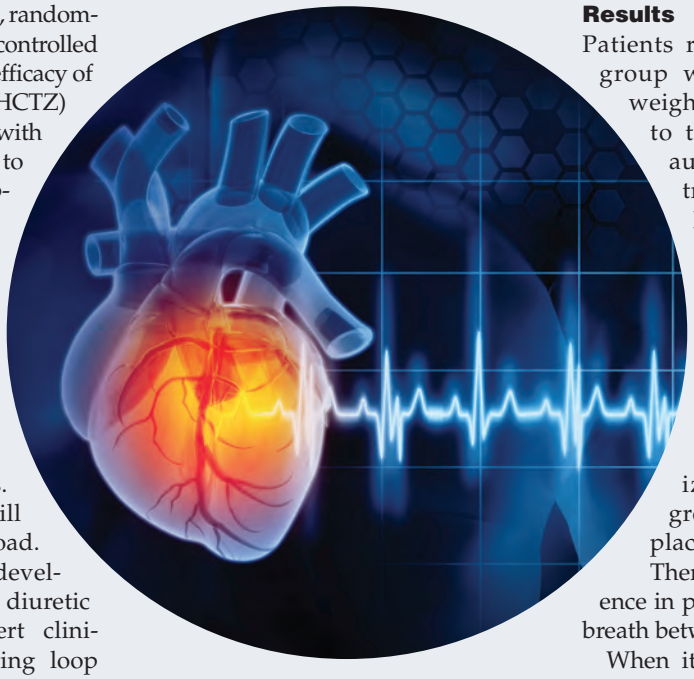
Based on the full body of literature examining the topic, BP management in hospitalized patients without signs of end-organ damage should focus on identifying underlying problems that may be causing secondary elevated BP, such as pain, anxiety, or the stress of being in a hospital setting. Once a potential cause is identified, clinicians can work to treat the underlying cause while avoiding use of medications—especially products given intravenously—that could lower BP. ■

Are there benefits to adding hydrochlorothiazide to loop diuretics for patients with acute heart failure?

Maya A. Harris, PharmD

Recent study findings highlight an alternative approach to combined diuretic treatment in patients with acute heart failure.

Researchers of a prospective, randomized, double-blind, placebo-controlled trial evaluated the safety and efficacy of adding hydrochlorothiazide (HCTZ) to I.V. furosemide in patients with acute heart failure. According to the findings, which were published in the February 2023 issue of *European Heart Journal*, the addition of HCTZ to loop diuretic therapy improved diuretic response in patients with acute heart failure.



Patients with acute heart failure are traditionally treated with loop diuretics. However, a small subset still struggles with fluid overload. This is due to resistance developed by long-term loop diuretic administration. Some expert clinicians recommend intensifying loop diuretic treatment prior to the addition of HCTZ, but study authors wanted to further explore the synergistic relationship between HCTZ and loop diuretics.

Study methods

The multicenter study included patients 18 years or older who had a history of chronic heart failure and had been hospitalized within the previous 24 hours for acute decompensated heart failure. Other criteria for eligibility included at least 1 month of treatment with oral furosemide 80 mg to 240 mg daily or an equivalent dose of a different loop diuretic.

Exclusion criteria included patients who were unstable upon admission, required renal replacement therapy, or were treated with inotropic agents or with thiazide diuretics 1 month before admission. Patients with low potassium and low sodium levels were also excluded if their values were less than or equal to 2.5 mmol/L and 125 mmol/L, respectively.

At each center, patients were randomized to receive oral HCTZ or placebo for 5 days, with HCTZ doses based on the current function of their kidneys. HCTZ doses were only adjusted to reflect the status of the kidneys. An algorithm based on the DOSE-AHF trial was used to determine the I.V. dose of furosemide. Patients were monitored for the duration of their hospitalization and for an additional 90 days after discharge.

The resulting patient population consisted of 230 patients averaging 83 years old, and 48% were female.

Efficacy outcomes included changes in body weight and patient-reported shortness of breath from baseline to 72 hours of randomization. Safety outcomes included changes in kidney function, low potassium levels, and low sodium levels. Impaired kidney function was defined as an increase in SCr by more than 26.5 µmoL/L or a decrease of more than 50% in serum eGFR. Low potassium levels and low sodium levels met the same criteria as mentioned above.

Results

Patients randomized to the HCTZ group were more likely to lose weight after 72 hours compared to the placebo group. Study authors found that patients treated with HCTZ lost 2.3 kg, while patients treated with the placebo lost 1.5 kg. Regarding patient-reported shortness of breath, there were no significant differences between groups. Similar trends were also observed after 96 hours of randomization, with the HCTZ group losing 2.5 kg and the placebo group losing 1.5 kg. There was no significant difference in patient-reported shortness of breath between groups.

When it came to kidney function, 46.5% of patients in the HCTZ group met the predetermined safety conditions compared to the 17.2% of patients in the placebo group. No significant changes were observed in potassium levels and sodium levels between the two groups.

Ultimately, the study authors found that the addition of oral HCTZ to I.V. loop diuretics does improve diuretic response, but at the expense of declining kidney function.

Takeaways

This trial is the first of this magnitude to study the safety and efficacy of oral HCTZ in acute heart failure. While the study authors' findings are consistent with current observational studies, these results emphasize a need to continue robust, prospective experiments to further explore potential adverse events of prolonged treatments in acute heart failure. ■

A minute with ...

Sridhar Rao Gona, MS, MHA, BSPharm
Clinical Pharmacy Informatics and Research
Meritus Medical Center, Hagerstown, MD
Member since 2021

"Being an APhA member has been an incredibly valuable experience for me. I've had the privilege of holding several leadership positions, including House of Delegates member and Special Interest Group member. My involvement in APhA has allowed me to contribute to important initiatives aimed at advancing the pharmacy profession. Overall, my APhA membership has been an essential part of my professional growth and has helped me make a meaningful impact on patient care. APhA is a vibrant and dynamic organization that provides pharmacists with opportunities to connect, learn, and grow in their profession."

How has APhA helped you establish meaningful connections?

As an APhA member, I've found the organization to be an invaluable resource for establishing meaningful connections within the pharmacy community, providing me with the opportunity to network with colleagues from all over the country and even internationally.

One of the most valuable aspects of being an APhA member is the access to resources and professional development opportunities. APhA provides members with the tools they need to stay current and advance their careers. I was able to leverage these resources to create meaningful programming for our members, which increased engagement and participation. Additionally, APhA membership has also provided me with opportunities to hone my leadership skills and advocate to make a positive impact in the profession. By serving in various positions, I've been able to advocate for policies that benefit pharmacists and their patients, such as expanding the role of pharmacists in health care and ensuring access to essential medications.

How does APhA help you thrive in your everyday practice?

APhA provides a wide range of tools and resources that have helped me to stay current in my field, improve my skills, and provide better care to my patients. Additionally, APhA helps me thrive in my everyday practice through its strong voice for pharmacists at the local, state, and national levels. By advocating for policies that support pharmacists and their patients, APhA has helped create a more favorable practice environment and increase recognition of the critical role that pharmacists play in health care.

What excites you about the profession of pharmacy?

I'm excited about the profession of pharmacy and the unique role it plays in improving patient health outcomes. Pharmacy is a constantly evolving field that provides a wide range of career opportunities. What excites me most is the opportunity to make a meaningful impact on patient health by providing personalized medication management and counseling, promoting medication adherence, and collaborating with other health care providers to optimize patient care.

I'm also excited about the potential for technology to transform pharmacy practice and improve patient outcomes.

Overall, the profession of pharmacy offers endless opportunities for professional growth and the satisfaction of making a positive impact on the health and well-being of patients.

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

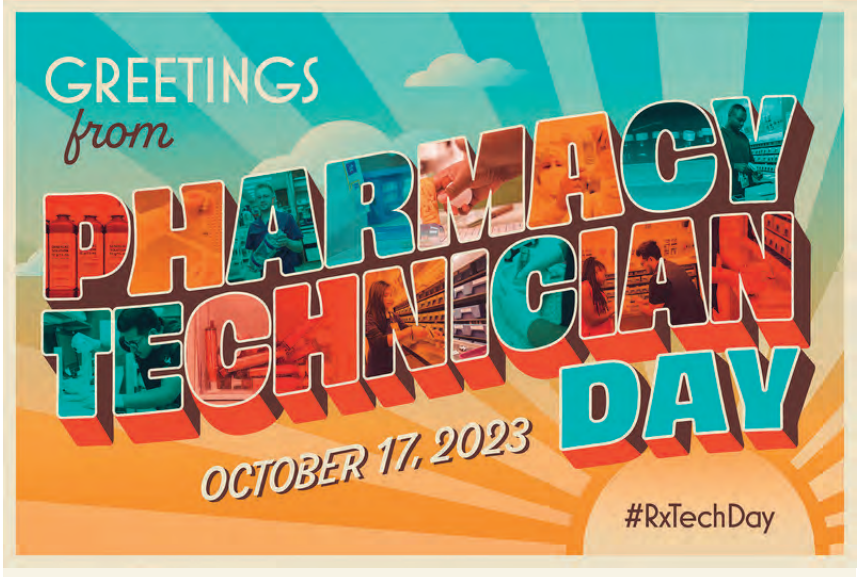
As a clinical pharmacy informatics researcher, I've had the opportunity to make a significant impact on patient care through my involvement in several research studies. One study that particularly stands out to me was focused on reducing adverse drug events in elderly patients by improving the monitoring process for digoxin toxicity. Through this study, we identified gaps in the current monitoring practices and developed a standardized approach for monitoring digoxin levels, resulting in reduced incidence of digoxin toxicity, improved patient outcomes, and reduced health care costs. This experience highlighted the importance of clinical pharmacy research and the potential for informatics to improve patient care. It was incredibly rewarding to see the impact of our work and to know that we were able to make a difference in the lives of patients. ■

Get involved in APhA

Interested in diabetes management? The Diabetes Management Special Interest Group (SIG) offers a support network of pharmacists and student pharmacists to connect and discuss up-to-date disease management information.

"Being part of the Diabetes Management SIG has provided resources and approachable networking opportunities to interact and collaborate with other pharmacists who are also passionate about diabetes management and actively providing care for people with diabetes in diverse settings and populations," said Bernadette Asias-Dinh, PharmD, clinical associate professor at Denver Harbor Family Health Center, in Houston, TX and SIG coordinator. "Whether it's working on a new business item that would benefit people with diabetes, increasing awareness of resources available to improve quality of care, or simply interacting with other pharmacists to share ideas and potential solutions to issues, I feel participation in this SIG ultimately helps progress the important role pharmacists have in diabetes management and ultimately improves patient outcomes."

Visit apha.us/DiabetesMGTSIG to learn more. ■



Did you know?

October 17 is Pharmacy Technician Day! Each year, the pharmacy community celebrates our pharmacy technicians! Some ways to show appreciation for the important work technicians do every day include

- Urging your pharmacy to purchase memberships in national and state pharmacy associations for technicians this month
- Decorating your pharmacy with graphics, badges, and more (found on PTCB's website at apha.us/PharmTechDay)
- Serving a special lunch event for pharmacy technicians and team members or bringing in sweet treats
- Making public announcements about Pharmacy Technician Day and the achievements of the technicians on your team ■

APhA advocacy

APhA and many other pharmacy organizations and associations convened to establish a Pharmacy Workforce Suicide Awareness Day to be recognized annually on September 20. September is Suicide Prevention Month.

If you are feeling alone and having thoughts of suicide—whether or not you are in crisis—or know someone who is, talk to someone you can trust by calling or texting "988," the Suicide & Crisis Lifeline.

Suicide is the twelfth leading cause of death for Americans (data from 2020). A recent study published by *JAPhA* showed that pharmacists are at an increased risk of death by suicide when compared to the general public. According to that same study, suicide rates among pharmacists in the U.S. are 20 per 100,000, which is greater than the general population of 12 per 100,000. Establishing a Pharmacy Workforce Suicide Awareness Day is an effort to increase awareness of and discussion around a highly stigmatized topic which disproportionately affects the pharmacy workforce. In addition, recognizing this day will support pharmacists, pharmacy residents, student pharmacists, and pharmacy technicians by providing resources to mitigate suicidal thoughts and mental health conditions.

Visit apha.us/SuicideAwareness for more information as well as helpful resources. ■

Responding to medication errors using a just culture approach in pharmacy practice

Ronald Zentz, RPh, DDS, FAGD, CPHRM, Consulting Director, CNA Specialty Risk Control, CNA Insurance, Chicago, IL, and **Georgia Reiner, MS, CPHRM**, Risk Analyst, Healthcare Providers Service Organization, Fort Washington, PA

An elderly, hypertensive patient in an assisted living facility received a new prescription for metolazone 2.5 mg. A local pharmacy which supplied most medications for residents of the facility received and filled the order. The assisted living facility staff administered the medication for approximately 3 weeks. During this time, the patient began to feel ill and became increasingly weak. Complaints of GI distress, nausea, vomiting, and, later, GI bleeding followed. The patient was hospitalized, and blood tests revealed severe pancytopenia. The hospital staff contacted the pharmacy to investigate the patient's preadmission medications, and discovered that the dispensed medication was methotrexate 2.5 mg. The patient's condition continued to decline and they expired soon after admission to the hospital.[1]

It is estimated that approximately 7,000 to 9,000 patients die every year in the United States due to medication errors, such as the one described in this case study.[2] In addition to these casualties, hundreds of thousands of others experience medication-associated adverse reactions or complications.

It is estimated that more than 1.5 million patients are harmed by medication errors every year in the United States.[3] Due to these errors, those patients and their loved ones can incur physical and psychological pain and suffering as well as significant financial damages. Cumulatively, these incidents also contribute to overall patient dissatisfaction and distrust in health care providers and institutions.

Although there is no uniformly accepted definition of a medication error, the National Coordinating Council for Medication Error Reporting and Prevention defines a medication error as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer."[4]

Medication errors can occur when there is a failure in one or more aspects of the medication use system—which includes health care procedures, systems, and products—including product labeling, packaging, and nomenclature. Medication errors also emanate from professional practice through medication prescribing, order communication, compounding, dispensing, distribution, administration, education, monitoring, and use.[4]

Pharmacists play a critical role in the prevention of medication errors as health care professionals whose role is intrinsic to the medication use system.

Addressing the problem of medication errors requires pharmacists to learn from mistakes and near-misses while using the experience to improve the systems and procedures that increase the risk of patient safety events. Interdisciplinary collaboration among all health care personnel is necessary to gain a full understanding of incidents that may lead to patient harm. By analyzing incidents that resulted in adverse outcomes for others, pharmacists can understand vulnerabilities and identify common causes of errors upon which to focus safety improvement initiatives.

Pharmacists must remain current on the types of medication errors that occur, steps to take in the event of an

Learning objectives

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

- Describe the impact of wrong-drug or wrong-dose errors in pharmacy.
- Define the "just culture" safety science framework as it relates to pharmacy and pharmacist regulation.
- Review best practices aimed at reducing medication errors in your pharmacy.
- Identify processes that should be followed when a medication error occurs.
- Recognize resources available for pharmacists related to medication safety and medication error prevention.

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. It is estimated that approximately how many patients die every year in the United States due to medication errors?

a. Between 1 million and 1.5 million
b. Between 7,000 and 9,000
c. Between 95,000 and 120,000
d. Between 35,000 and 50,000

2. National Coordinating Council for Medication Error Reporting and Prevention defines a medication error as

a. Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer
b. Any response that is noxious, unintended, or undesired, which occurs at doses normally used in humans for prophylaxis, diagnosis, therapy of disease, or modification of physiological function
c. An unexpected occurrence involving death or serious physical or psychological injury, or the risk thereof. Serious injury specifically includes loss of limb or function. The phrase "or the risk thereof" includes any process variation for which a recurrence would carry a significant chance of a serious adverse outcome
d. Any error, adverse drug event, and medication misadventure that causes significant morbidity or mortality and are possibly preventable

3. According to the third edition HPSO/CNA Pharmacist *Claim Report* analysis, the average total incurred for claims alleging that the wrong drug was dispensed increased to an average of

a. $82,528
b. $94,194
c. $110,821
d. $127,233

error, and resources available to help mitigate risk. To that end, we aim to describe the most commonly occurring medication errors in pharmacy and to review best practices designed to reduce them.

Essential to this goal is the implementation of a "just culture" safety science framework as it relates to pharmacies and pharmacists. We also identify processes that should be followed when a medication error occurs. Finally, we will recognize and refer to resources available to enhance medication safety and error prevention.

An update on medication errors in pharmacy practice

The *Pharmacist Professional Liability Exposure Claim Report: 3rd Edition* (*Claim Report*), published in September 2023 by CNA and Healthcare Providers Service Organization (HPSO), identified and addressed liability exposures incurred by its insured pharmacists and pharmacies.[1] Supported by APhA and with input from the Institute for Safe Medication Practices (ISMP), the *Claim Report* contains an analysis of pharmacist professional liability (i.e., malpractice) claims that closed from 2017 to 2022 and incurred a payment of $1 or more as a result of a claim settlement or judgment. The *Claim Report* found that wrong-drug and wrong-dose/strength errors comprise the greatest distribution of allegations in professional liability closed claims, reflecting 41.7% and 21.9% of all pharmacist malpractice claims, respectively (Figure 1).[1] Similar reports produced in 2013 and 2018 also concluded that wrong-drug and wrong-dose/strength errors comprised the greatest percentage of allegations in pharmacist professional liability closed claims.[5,6]

The *Claim Report* found that the average total incurred (i.e., the sum of all monies paid on behalf of an insured pharmacist to manage, defend, and resolve a claim) for claims alleging that the wrong drug was dispensed increased 16.3% compared to the *Pharmacist Liability Claim Report: 2nd Edition* (*2nd Edition Claim Report*), increasing from an average of $80,974 per claim to an average of $94,194.[1]

Factors affecting wrong-drug dispensing errors in the *Claim Report* most often included failure to prevent look-alike and sound-alike (LASA) drug errors and failure to check the drug against the label and actual prescription (Figure 2).[1] The *Claim Report* found over 60 unique combinations of drugs involved in closed claims alleging wrong-drug errors, with the drugs most commonly involved in wrong-drug allegations being methadone, dexlansoprazole, gabapentin, and metformin.[1] While technology can help prevent medication errors such as LASA errors, over-reliance or complacency with these tools can still allow errors to occur.

Medication errors also may originate at any point during the medication use process. Although wrong-drug errors may

Figure 1. Distribution of closed claims by top 5 most common allegations

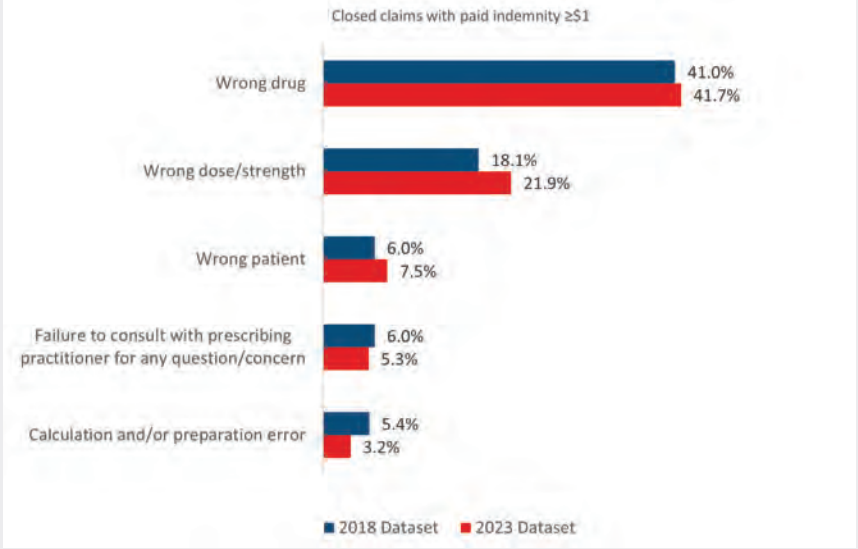


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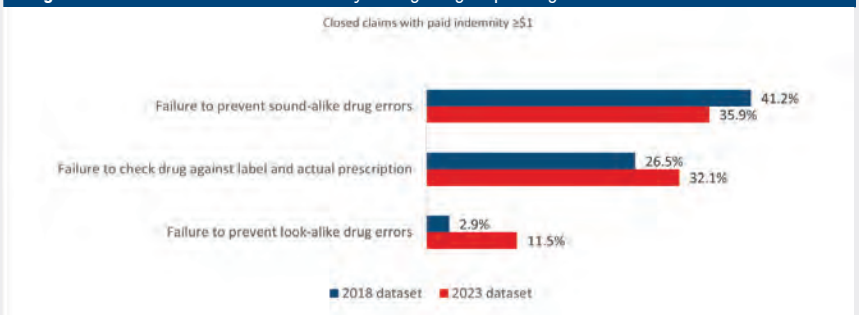
Figure 2. Distribution of closed claims by wrong-drug dispensing errors



Adapted from Reference 1.

not always originate with the pharmacist, they may still lead to allegations against the pharmacist, such as allegations of a failure to determine whether a medication could have an adverse interaction with a patient's existing medication profile.[1] During the medication dispensing phase, pharmacies and pharmacists have the opportunity to identify and prevent wrong-drug errors as well as errors associated with patient allergies and contraindications by employing strategies such as ensuring sufficient staffing levels, implementation of bar code scanning, and offering and conducting patient counseling.[1]

Wrong-dose/strength claims exhibited a 46% increase in the average total incurred per claim since publication of the *2nd Edition Claim Report*.[1] The average total incurred per claim in this category rose from $49,901 to $72,972.[1] Several high-severity claims, including two cases of permanent organ injury and one patient death, contributed to this increase.[1] Wrong-dose/strength errors, such as those examples described in Table 1, most often involved either the wrong strength of product being dispensed; a 10-fold overdose being dispensed; or the product strength dispensed being correct, but erroneous patient instructions resulted in an incorrect dosage.[1] The *Claim Report* demonstrated that wrong-dose/strength errors are most often associated with one or more human errors and environmental factors, such as workplace distractions and understaffing, misinterpretation of a prescription, selecting the wrong medication from the computer screen listing, or pulling the incorrect medication strength from the shelf.[1] Use of certain error-prone abbreviations, symbols, and dose designations also may contribute to medication errors, whether used in written, verbal, or electronic communications.[7] A prescriber also may provide the pharmacy with an incorrect strength or dose frequency order in the prescription, and the pharmacist, in turn, may not catch the error.[1]

Several wrong-dose/strength errors identified in the *Claim Report* involved high-alert medications, often resulting in severe patient injuries.[1] (Refer to the section below on targeted practices for more information on high-alert medications.) Although the *Claim Report* could not conclude whether or not pharmacist-closed claims are more commonly associated with high-alert medications, it was able to confirm that the potential consequences for failing to prevent these errors are significant and often devastating.[1]

A just culture approach to improving medication safety

To improve medication safety, leaders in the pharmacy industry and profession have taken steps to advocate for more organizations to follow a just culture safety science framework. Many states and state boards of pharmacy are working to improve patient safety by introducing just culture concepts and encouraging the reporting of medication errors and near-miss events in an environment that focuses on learning and advancing the profession.[8]

The APhA House of Delegates adopted six policies in 2023 related to the just culture approach to patient safety with the aim of supporting pharmacy professionals and reducing medication errors.[9]

As described later, ISMP released a guide on targeted medication safety and best practices for community pharmacy in 2023 to help prioritize and mobilize adoption of best practices to improve patient safety and avoid harmful or fatal medication errors.[10] It follows that pharmacists should learn to recognize how a just culture approach to patient safety can support pharmacy professionals and help reduce the frequency and severity of medication errors.

Table 1. Drugs involved in multiple wrong dose/strength closed claims by dose/strength prescribed versus dispensed

Drug	Dose prescribed	Dose dispensed	Resulting injury or adverse event
Aripiprazole	2 mg once daily	20 mg once daily	Emotional/psychological distress
Aripiprazole	2 mg once daily	20 mg once daily	Tremors, tardive dyskinesia
Aripiprazole	5 mg once daily	30 mg once daily	Altered mental status, hospital admission for observation
Amitriptyline	10 mg	100 mg	Lethargy, dizziness
Amitriptyline	10 mg	100 mg	Lethargy, dizziness, syncope, requiring hospitalization
Amitriptyline	25 mg	100 mg	Lethargy, dizziness, vertigo
Morphine	20 mg/5 mL every 4 hours as needed	100 mg/5 mL every 4 hours as needed	Drowsiness, altered respirations, hospital admission for observation
Morphine	20 mg/mL, 0.5 mL every 6 hours as needed	20 mg/mL, 1/2 tsp (2.5 mL) every 6 hours as needed	Drowsiness, altered respirations, hospital admission for observation
Morphine (extended release)	30 mg	60 mg	Drowsiness, GI distress
Tacrolimus	5 mg once every 12 hours	0.5 mg once every 12 hours	Swelling, kidney rejection symptoms, requiring hospitalization (minor patient)
Tacrolimus	0.5 mg, take 5 capsules every 12 hours	5 mg, take 5 capsules every 12 hours	Renal failure
Vitamin D	1,000 units daily	50,000 units daily	Emotional/psychological distress
Vitamin D	50,000 units, take once per week for 4 weeks	50,000 units, take once per day for 4 weeks	Emotional/psychological distress
Warfarin	1 mg, take 5 daily	5 mg, take 5 daily	Prolonged clotting time
Warfarin	2 mg, one tablet on M-W-F, take two tablets on other days	5 mg, one tablet on M-W-F, take two tablets on other days	Brain hemorrhage, hospitalization, death

An organization that adheres to a just culture framework is guided by a commitment to shared responsibility and accountability across all levels and disciplines within the organization in order to identify solutions to patient safety issues. This framework also recognizes that humans are not infallible, though they are not necessarily the main source of safety issues.

Addressing patient safety issues requires that systems, including medication use systems, be designed to discourage risky human behaviors and reduce the risk of systems errors.[11] Thus, advancing patient safety efforts requires that individuals be encouraged, and rewarded, to report errors and near-misses so that lessons can be learned and systems can be further improved.[11,12] Rather than simply blaming the individual(s) involved in an error, the focus is placed on identifying and addressing the environmental and procedural factors that encourage individuals to engage in unsafe behaviors and permit errors to occur.

Differentiating between behaviors associated with medication errors

Critical to the just culture concept is the recognition that important distinctions exist between the types of behaviors that contribute to errors.[12] An organization committed to a just culture distinguishes between human error, at-risk behavior, and reckless behavior.

Organizations adhering to a just culture framework calibrate their response to an error or near-miss based upon the behavior associated with the error rather than the severity of the incident or outcome (Table 2).[12]

In a just culture framework, identifying the differences between these behaviors, their causes, and motivations helps pharmacy leaders set realistic expectations and promote accountability within the pharmacy.[3] Often, human resource–related policies and procedures fail to establish a disciplinary process that supports education, patient safety, and improvement.[13] Organizations typically view any breach of policies, procedures, or standards of practice that led to an error as cause for disciplinary action, even in circumstances in which a breach may be due to system failures, environmental factors, and/or commonly

Table 2. Behaviors associated with medication errors

Behavior	Human error	At-risk behavior	Reckless behavior
Definition	Unintentional, unavoidable, and unpredictable failures in the ways we all interpret, think, and act	Intentional choices based on the assumption that the risk associated with the choice is insignificant or justifiable, or behaviors that have become the norm within a group	Intentional, conscious disregard of obvious, substantial, and unjustifiable risk
Examples	Transposing the numbers in a medication dose, mishearing a telephone prescription order, or selecting the wrong drug from a drop-down menu	Overriding automated alerts, scanning one container several times for multiple containers of the same drug, or dispensing an unknown medication	Drug diversion, acts of retaliation, working under the influence of alcohol or drugs on the job, or continuing to engage in at-risk behavior despite coaching
Motivation	"None; these mistakes are not intentional behavioral choices"	Typically believe they are making a relatively "safe" choice based on a genuine desire to help others, such as patients or colleagues	"Prioritizing individual wants/needs above the safety of others; in some cases, driven by a behavioral health issue such as an untreated substance use disorder"
How to address	Console the individual(s) involved and engage them in training. Redesign systems to implement multiple strategies that reduce or eliminate risk.	Coach the individual(s) involved on the risks associated with their behavior. Reward safe behaviors. Evaluate and redesign systems to reduce or eliminate risk.	"Punish reckless behaviors by taking swift, appropriate disciplinary action in accordance with HR policies and statutory requirements, as applicable. In some cases, the response may involve legal action."

Source: Adapted from References 3 and 13.

employed workarounds.[13] However, understanding the underlying human and systemic factors that may lead to errors can help pharmacists prevent errors through a just culture approach that prioritizes education, training, and system improvements.

Human error

First, it's important to distinguish between intentional acts and human error.

We are all prone to mistakes and are influenced by factors including inherent biases, psychosocial factors, our environment, and the systems within which we work. As a result, human errors are inevitable and unpredictable. They are not behavioral choices or intentional actions; instead, human errors reflect failures in the way we perceive, think, or act.[13]

Human error may include mistakes such as accidentally adding an extra zero to the end of a number, selecting the wrong vial from two look-alikes, or selecting the wrong drug from a drop-down menu.

Human error is typically the fault of systems that permit these types of errors to occur due to a failure to consider human fallibility.[3] Within a just culture framework, responses to human error should primarily focus on redesigning and improving systems to reduce or eliminate risk, when possible, rather than punishing the individual(s) involved in the error.

Organizations should implement multiple strategies to address sources of error, including automation, standardization, forcing functions, and failsafes.[13]

The potential or actual severity of the error should not influence how the individual who made the error is treated.[13] Pharmacists and pharmacy staff deserve the assumption that their intentions were good. They should be provided with empathetic, nonjudgmental, respectful support in the aftermath of an error.[14,15] There should be opportunity to learn from mistakes without fear of punishment and to contribute to improving systems to prevent future errors.[3,13]

At-risk behavior

Unlike human error, at-risk behaviors are intentional choices. These behaviors typically occur either when there is an assumption that the risk associated with a specific choice is insignificant or justifiable, or when a behavior has become a norm within a group (sometimes referred to as a "workaround").[13]

While those who have less experience in a particular role or organization may be more prone to human error as they acclimate to new systems, more experienced individuals tend to be more likely to exhibit at-risk behaviors. When exhibiting at-risk behavior, individuals become less attentive to the importance of adhering to policies and procedures, relying more on workarounds and shortcuts to complete their work.[13]

At-risk behaviors, including workarounds and overrides, are often viewed as a necessary adaptation to poorly designed systems or inadequate resources; for example, in situations involving burdensome productivity metrics, inadequate staffing, or slow or buggy technology.[15]

Additional considerations: Compounding

Notably, 9.6% of claims in the *Claim Report* were attributed to compounding pharmacy errors, with an average total incurred ($438,221) more than three times the overall average of $136,000 per claim.[1] These findings emphasize the importance of risk mitigation for both sterile and nonsterile medication compounding services to prevent serious adverse outcomes.

Although best practice recommendations for medication compounding are beyond the scope of this article, it is important that pharmacists and all members of the health care team remain vigilant to ensure that compounded medications, when required for specific patient needs, are prepared and delivered safely and accurately in order to minimize errors and unintended consequences. Note that a primary best practice is to use commercial products that meet patient needs rather than compounded products whenever possible. The following resources may aid pharmacists in compounding risk mitigation efforts.

- FDA: Human drug compounding: www.fda.gov/drugs/guidance-compliance-regulatory-information/human-drug-compounding
- FDA: Compounding questions and answers: www.fda.gov/drugs/human-drug-compounding/compounding-and-fda-questions-and-answers
- USP Compounding Compendium: Quality assurance resource for compounding methods, and practices: www.usp.org/products/usp-compounding-compendium
- American Society of Health System Pharmacists: Compounding frequently asked questions: www.ashp.org/-/media/assets/advocacy-issues/docs/compounding-guidances-frequently-asked-questions.pdf
- American Society of Health System Pharmacists: Compounding Resource Center: www.ashp.org/pharmacy-practice/resource-centers/compounding
- Board Certified Sterile Compounding Pharmacist credential: www.bpsweb.org/bps-specialties/compounded-sterile-preparations-pharmacy/
- ISMP: Guidelines for Sterile Compounding and the Safe Use of Compounding Technology (2022): www.ismp.org/resources/guidelines-sterile-compounding-and-safe-use-sterile-compounding-technology
- APhA: Compounding resources page: www.pharmacist.com/Practice/Patient-Care-Services/Compounding

There is also a perception that the likelihood of being caught and punished for engaging in these types of at-risk behaviors is relatively low, while the perceived benefits of risk taking are immediate.[3]

Of the three categories of behaviors that contribute to errors, at-risk behaviors should be the primary focus for pharmacies and other health care organizations. They represent the greatest patient safety challenge as well as the greatest opportunity to improve systems.[13]

To address these at-risk behaviors, organizations must be transparent with staff about error trends and system failures and engage employees to promote patient safety best practices. Pharmacies should involve pharmacists and pharmacy staff in redesigning systems, which in turn will help encourage them to be more accountable for their actions and for addressing problems as they arise.[3]

In addition, it is just as important to reward those who continuously meet patient safety goals and report near-misses as it is to coach those who engage in at-risk behaviors.[3]

Working within a just culture framework means valuing continuous learning, treating health care workers with dignity, respecting their expertise and input, and working with them to identify risks and solutions to mitigate risk.[11] It is not sufficient to place these types of sentiments and policies on paper. Rather, pharmacists and pharmacy staff must intrinsically feel supported by organizational leadership as they work toward shared patient safety goals. Enhancing patient safety measures and reducing medication errors must be the north star that guides all organizational decision-making.[3]

Reckless behavior

The final category of behaviors associated with medication errors is reckless behaviors. Recklessness involves an intentional disregard for an obvious, unjustifiable risk.[13]

Unlike those who engage in at-risk behaviors, those who engage in reckless behaviors know that their behavior presents a substantial, indefensible risk of harming others.[13] However, those who engage in reckless behaviors nonetheless make a conscious choice to disregard that risk in the interest of helping themselves and addressing their own needs and desires.[13]

Reckless behavior may include actions such as drug diversion; acts of retaliation against the organization, coworkers, or patients; working under

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the influence of alcohol or drugs; or continuing to engage in at-risk behavior despite repeated coaching.[13]

Considering the severity of these types of transgressions and the motivations behind them, responses to reckless behavior necessitate disciplinary action according to human resources policies. In some cases, legal action may be pursued against those involved, as appropriate per applicable statutes, regulations, and advice of legal counel.[3] Moreover, organizations should evaluate system redesign or enhancements to help curb the risk of similar reckless behaviors in the future.

Pharmacies should establish an anonymous reporting system for staff to report concerns, including a standard, confidential process for investigating alleged drug diversion. The ISMP has several resources addressing the topic of drug diversion available through its website, including webinars and newsletters.[1,16,17]

In some cases, reckless behavior may result from an untreated (or undertreated) behavioral health issue, such as a substance use disorder or addiction.[18] Addiction, as a disease, can cause physical changes to the areas of the brain essential to regulating decision-making and judgment.[19] Therefore, some of those who experience substance use disorders engage in reckless behaviors in pursuit of drug or alcohol use, such as engaging in substance use at work or diverting medications for personal use.[18,19] Although these facts and circumstances do not exempt anyone from facing appropriate consequences for their actions, it does also indicate that even some cases of reckless behavior should be addressed with a degree of compassion. In these cases, referral to a local professional pharmacists' recovery network and/or an employee assistance program may be appropriate.[20] This referral permits a challenged pharmacist to seek confidential help and enter recovery, so that they may one day continue to practice safely.

Reducing medication errors: Priorities and actions

The *Claim Report*'s closed claim data summarized previously identifies common error types. This information—as well as other industry reports and findings from professional and safety organizations, government agencies, and other reputable sources, such as the ISMP and the FDA MedWatch reporting system—may aid pharmacists and pharmacies in prioritizing risk mitigation strategies to improve processes, procedures, and safety measures and to prevent patient harm.[21]

Targeted best practices

In 2023, ISMP introduced its first targeted medication safety best practices for community pharmacy ("ISMP Best Practices").[10] These five consensus-based recommendations and the associated Best Practices Worksheet focus on preventing serious and fatal medication errors.[22] A similar publication is also available for the hospital setting.[23]

The areas of emphasis and guidance are generally consistent with the types of errors and injuries in the *Claim Report*. Moreover, proposed risk mitigation strategies help to address human error and at-risk behaviors described previously and presented in Table 2. Consequently, the ISMP Best Practices are summarized here and serve as an evidence-based approach to medication error reduction.

The items are delineated based upon the potential impact on top allegation categories as identified in the *Claim Report*. Readers are strongly encouraged to obtain and review the full document for further details and to consider other resources in order to identify methods and priorities that align with the goals of your team and organization.

1. Barcode verification technology

Install and use barcode verification during the prescription filling process.

Scan the medication package or container (which may include containers from which the medication is removed to fill a prescription, or those that may be directly dispensed to a patient).

Develop a workflow process that requires the generation of labels and the filling of prescriptions for one patient before printing labels and working on prescriptions for another patient.

Regularly review metrics to assess effectiveness and compliance rates. In a busy practice setting, workarounds may diminish the safety improvements that could be realized from utilization of a bar code verification, such as reverting to manual entry processes or scanning from a sheet of frequently used barcodes rather than from the medication label.

Effective team communication and transparency are integral to identifying and eliminating adherence barriers and preventing workarounds.[10]

Comments

This best practice may significantly reduce the most frequent types of errors reported in the *Claim Report*: those involving a wrong drug, wrong dose/strength, or the wrong patient.[1]

Although barcode technology may increase efficiency and improve safety in health care settings, its use in pharmacies is not universal.

Pharmacists and pharmacies may wish to consult a complementary, comprehensive "readiness assessment" tool to help identify barriers and facilitate the implementation of barcode technology.[24] This tool engages both pharmacy leadership and staff in the assessment process, noting that a team approach is necessary for the implementation of any significant system change.

Collaboration is consistent with a just culture system of accountability and—not surprisingly—a "culture of safety" features prominently in the readiness assessment.[24]

LASA or confused drug errors represent a significant subset of wrong-drug errors in the *Claim Report*.[1] The *Claim Report* revealed that confused drug errors or medication mix-ups comprised the most common type of wrong-drug error (approximately 45%) in both the current and previous claim reports.[1]

Although barcode scanning is a very effective mitigation strategy, it is important to remember that no single strategy will successfully eliminate medication errors.

In a January 2023 featured article, ISMP explains some of the history and methodologies employed to differentiate look-alike medications, such as tall man (i.e., mixed-case) lettering and

bolded text.[25] Based in part on a 2022 survey of pharmacists, nurses, pharmacy technicians, physicians/prescribers, and other professionals, the 2023 update to the FDA and ISMP medication lists provides the latest guidance for the use of tall man (i.e., mixed case) letters to help prevent confused medication errors.[25,26]

Readers should also note and refer to the ISMP's List of Confused Drug Names.[27] This list includes LASA medication name pairs and can assist pharmacists with identifying medications that may require special safeguards to mitigate the risk of errors; for example, including both brand and generic names as well as the indication for use on prescription orders or setting up computer systems to separate and/or alter look-alike medication names on the computer system display to help decrease the risk of selection errors.[27]

2. Standardize liquid measure

Use the milliliter (mL) unit of measure for all liquid medication activities, including prescribing, measuring, and dispensing.

Implement metric directions and dosing devices. Eliminate references to "teaspoonful," "tablespoonful," and other nonmetric/nonstandardized units of measure.

Dispense a metric-only dosing device that most closely matches the prescribed dose volume. Counsel and educate patients on how to measure doses accurately and use the "teach-back" method to confirm their understanding.[10]

Comments

Patients, parents, and other caregivers may have low health literacy, and as a result may not understand the benefits associated with the use of a standardized liquid measure. One systematic review found that more than two-thirds of parents had low to marginal health literacy.[28] Although over 70% of parents believed mL-only dosing to be easy, approximately 30% felt it was difficult or had no prior experience using the metric mL measurement.[27]

Confirming patient or caregiver understanding is a critical component of risk mitigation for liquid medications. For more information and pharmacy-oriented health literacy tools, consider consulting the AHRQ Pharmacy Health Literacy Center on AHRQ.gov.

3. Oral methotrexate dose/high-alert medications

The ISMP Best Practices emphasize the implementation of measures to prevent oral methotrexate dose errors and severe/fatal adverse outcomes.[10] Note that the *Claim Report* includes a number of severe claims and patient deaths associated with several other high-alert medications, in addition to oral methotrexate.[1] Therefore, additional high-alert error mitigation actions are proposed below.

ISMP Best Practices to prevent oral methotrexate dose errors include, but are not limited to, incorporating a default weekly dose regimen in electronic medication systems, requiring verification and entry of an oncologic indication for daily dosing, and requiring pharmacist–patient or –caregiver education for all oral methotrexate prescriptions.[10]

Patients should receive clear written and verbal instructions on the dosing schedule, with emphasis on the dangers associated with taking more medication than prescribed. Use strategies such as "teach-back" (patients repeat the instructions/dosing schedules) to confirm understanding.

Comments

A wrong-drug error referenced in the *Claim Report* involving oral methotrexate was previously described. Another case included in the *Claim Report* dataset involved a prescriber error that was overlooked by the pharmacist (daily administration rather than weekly).[1]

Although not described in the *Claim Report*, it is interesting to note that the physician and pharmacist settled the claim with the deceased patient's family separately. The total incurred for the insured pharmacist exceeded $650,000. The physician case's outcome was unknown.

These two claim cases exemplify the risks associated with oral methotrexate prescriptions and the reason for an emphasis on this medication in the ISMP Best Practices.[10] However, oral methotrexate represents one of many high-alert medications implicated in severe adverse outcomes. Therefore, it is important for pharmacists and pharmacies to consider the risks involved with all high-alert medications and implement controls to prevent serious adverse outcomes.

Initially published in 2008, the latest High-Alert Medications in Community/Ambulatory Care Settings list includes medications that bear a heightened risk of significant patient harm in the event of a medication error.[29] ISMP has published similar lists for long-term care and acute care settings. These documents may be accessed at ISMP.org/recommendations.

High-alert medication cases included in the *Claim Report* involve anticoagulants, insulins, opioids, sedation agents, immunosuppressant agents, sulfonylurea agents, and others.[1] This underscores the need to remain vigilant and to implement strategies to mitigate the associated risks.

Additional high-alert medication safety strategies to consider include

- Implement a secondary labeling system and automated warnings for high-alert medications.
- Limit access to high-alert medications to appropriately trained staff as much as possible.
- Consider a manual independent review, automated double-checks, and other verification safeguards.
- Use electronic hard stops at the point of sale to require patient counseling and education before dispensing high-alert medications or when dispensing to high-risk patient populations.
- Ensure that pharmacy computer systems incorporate critical alerts for narrow therapeutic index and high-alert medications. Establish a protocol to confirm regular system updates.
- Utilize pharmacy computer systems that are designed to perform dose range checks and that alert staff regarding potentially dangerous doses (e.g., overdose or subtherapeutic levels) for medications with

a narrow therapeutic index and high-alert medications.
- Provide annual pharmacy staff education, at a minimum, on ways to avoid errors with high-alert medications and other error-prone medications or devices.
- Incorporate medication safety discussions into regular team meetings. Review near-misses, successful safety process improvements, and medication safety resources.

4. Confirm patient ID

Implement a standard procedure/protocol to verify patients' identity (ID) that utilizes at least two patient-specific identifiers.

ID verification should apply not only when receiving a prescription to be filled, but also for other touchpoints such as responding to patient-specific questions, medication delivery, and prior to vaccine administration or other treatments. Pharmacy personnel should confirm that identifiers are consistent with the prescription and information available in the pharmacy's electronic information system.

Point-of-sale technology solutions can require that ID confirmation takes place before transaction completion.[10]

Comments

Wrong-patient errors continue to be a significant concern across pharmacy practice settings. Although this error type ranks third in the *Claim Report* error distribution (Figure 1), the average total incurred has increased from $84,947 to $88,054 since the *2nd Edition Claim Report*.[1,5]

Importantly, according to the ISMP Best Practices, this error type tops the list of complaints received by the ISMP National Consumer Medication Errors Reporting Program.[30]

Additional data suggest that this error type may occur at least once for every 1,000 prescriptions.[31]

5. External medication safety resources

Seek out external resources and information about medication errors and safety risks. Use this knowledge to educate internal team members and to develop methods to mitigate risks and prevent errors in your professional practice/pharmacy.

Share and discuss near-miss occurrences, medication errors, and the resulting system improvements. Make medication safety a regular/daily topic of staff huddles and team meetings.[10]

Comments

A key "take-home" message for the prevention of medication errors is that success requires awareness, intention, and diligence. Building a culture of safety throughout an organization and among all team members promotes accountability—to the team, the organization and to the public we serve—and facilitates success toward realizing a safer medication delivery system.

Post-medication error actions

Establishing a culture of safety must include a mechanism for learning from errors as part of continuous improvement. This requires the implementation of written policies and procedures that facilitate error identification, investigation, corrective action, and reporting.

Taking appropriate action will help to mitigate the risk of future errors and patient injuries. Furthermore, pharmacies and pharmacists should understand and comply with applicable federal and state laws and regulations for required quality assurance programs and activities.

It is also important to understand and confirm whether regulations in your state or jurisdiction protect quality assurance/peer-review documents and work products from legal discovery in the event that a medication error leads to the filing of a malpractice lawsuit. Advice of legal counsel should be sought on this issue.

Consider the patient first

As a health care professional, the pharmacist's first priority should be the patient's safety and well-being. When appropriate, take actions necessary to ensure prompt medical referral or emergency treatment.

Apart from the patient's medical needs, it is imperative that pharmacists are skilled in how to communicate transparently with patients, especially during times of crisis following a medication error. Transparent communication with the patient, family, and/or caregiver regarding the event enhances trust and minimizes misunderstandings that often lead to litigious actions.

Emphasize facts during the discussion, focusing on what is known to have occurred. Be honest with the patient and do not speculate about anything unknown. Express sympathy without assigning blame or criticizing anyone who may have been involved in the event. Importantly, be prepared to answer questions about what steps will be taken to prevent such events in the future.

Workshops on effective communication and difficult patient discussions will help pharmacy personnel to effectively manage these challenging situations. Consider accessing and utilizing AHRQ training materials, such as the Communication and Optimal Resolution Toolkit available at AHRQ.gov.

After immediate medical concerns and patient notification are addressed, the following general risk management steps should be implemented. Note that the scope and order of these steps may vary depending upon the pharmacy or organization's internal procedure or protocol.

- Notify appropriate internal personnel (e.g., pharmacy manager, supervisor, risk manager, pharmacy owner, or others per the organizational procedure) and the prescriber.
- Secure/quarantine any equipment, medications, active ingredients, or supplies involved in the event.
- Document the error in the patient's profile.
- Understand and comply with any federal, state, and jurisdictional mandatory medication error reporting requirement(s) that may apply to the incident.
- Consider notifying the professional liability insurer(s) of the pharmacist and/or pharmacy about the incident, even if a claim or lawsuit has not been asserted or filed. At a minimum, understand when notification is required under the

policy's provisions.
- Consider reporting to anonymous voluntary reporting programs to help prevent similar errors from occurring at other organizations.[30,32]

Investigation

The next step is to review and initiate the organization's error investigation plan/process.

An investigation should be initiated immediately or as soon as possible after the event. Immediate investigation helps to preserve accuracy, as memories fade and perceptions of details vary over time. Investigative findings should be documented on a separate form specifically used for quality and performance improvement activities.

The scope of the investigation may depend upon the incident type and event severity. The individual responsible for receiving and managing adverse event reports should conduct the initial investigation and determine next steps.

If no such procedure exists, consider referring to ISMP's Assess-ERR™ Medication System Worksheet as one approach.[33] Community pharmacy and medical facility worksheet versions are available.[33] The worksheets are a component of a comprehensive workbook designed to assist pharmacists and other pharmacy personnel in identifying system gaps and weaknesses to facilitate safety improvements.[34]

If it is appropriate for your organization, consider the incorporation of a root cause analysis (RCA) process to identify the system/process issues underlying the medication error incident. An RCA process typically involves a cross-functional team to determine an error's root cause. In one of the most common approaches, "why" is asked repeatedly when analyzing the human, process, and systems failures that led to the incident until all contributing factors and a root cause are known. The information obtained should identify factors that led to the event so that corrective actions may be taken to prevent a recurrence of similar issues.

Two complimentary and easily available RCA resources focused on health care settings are offered that may align with the needs or your organization.[35,36]

Medication error reports should include factual, objective information regarding the event. The report should not include statements regarding blame or admissions of liability.

When completed, the report should be reviewed by the individual responsible for managing the error reporting process as well as organizational and clinical leaders.

Follow-up

Educational programs for pharmacists and pharmacy staff should be ongoing and include information regarding patient safety, medication errors, the investigative process, and patient safety enhancements as an outcome of the process. Education for those responsible for the investigative process should include the importance of investigative objectivity, interviewing skills, use of open-ended questions, and keen listening skills.

In pharmacy or in any health care setting, silence can be fatal. All health care professionals and team members should be ready to speak up and raise questions regarding a possible error or safety risk. A readiness checklist may be downloaded and utilized as part of your organization's safety education and training efforts.[37]

Conclusion

Medication errors are usually preventable events. Pharmacists and other pharmacy personnel must be knowledgeable about the types of potential errors that may occur and must exercise skill and due care in their daily work. A personal commitment to continuing education and being open to changes that will improve safety and risk management represent important steps along this path.

Pharmacy professionals, pharmacy owners, and business leaders must honestly and critically evaluate their own systems and procedures in order to recognize safety issues and implement corrective actions. A team approach to corrective action development in a just culture framework is paramount in helping to maximize effectiveness and buy-in for new or modified policies or procedures.

Encouraging and developing a culture based upon open communication and being receptive to constructive feedback and recommendations from the team and patients are critical to realizing medication error and patient safety improvements. Dedication and commitment to this goal will help to ensure patient safety and avoid reputational risk that may ensue in the event of an adverse outcome.

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CPE information

To obtain 1 hour of CPE credit for this activity, complete the CPE exam and submit it online at www.pharmacist.com/education. A Statement of Credit will be awarded for a passing grade of 70% or better. You have two opportunities to successfully complete the CPE exam. Pharmacists and technicians who successfully complete this activity before October 1, 2026, can receive credit. Your Statement of Credit will be available online immediately upon successful completion of the CPE exam.

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

To claim credit

1. Go to http://apha.us/CPE1023.
2. Log in to your APhA account, or register as a new user.
3. Select "Enroll Now" or "Add to Cart" (click "View Cart" and "Check Out").
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Assistance is available Monday through Friday from 8:30 am to 5:00 pm ET at APhA InfoCenter by calling 800-237-APhA (2742) or by e-mailing infocenter@aphanet.org.

CPE Assessment

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

1. It is estimated that approximately how many patients die every year in the United States due to medication errors?
- a. Between 1 million and 1.5 million
- b. Between 7,000 and 9,000
- c. Between 95,000 and 120,000
- d. Between 35,000 and 50,000

2. National Coordinating Council for Medication Error Reporting and Prevention defines a medication error as
- a. Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer
- b. Any response that is noxious, unintended, or undesired, which occurs at doses normally used in humans for prophylaxis, diagnosis, therapy of disease, or modification of physiological function
- c. An unexpected occurrence involving death or serious physical or psychological injury, or the risk thereof. Serious injury specifically includes loss of limb or function. The phrase "or the risk thereof" includes any process variation for which a recurrence would carry a significant chance of a serious adverse outcome
- d. Any error, adverse drug event, and medication misadventure that causes significant morbidity or mortality and are possibly preventable

3. According to the third edition HPSO/CNA Pharmacist *Claim Report* analysis, the average total incurred for claims alleging that the wrong drug was dispensed increased to an average of
- a. $82,528
- b. $94,194
- c. $110,821
- d. $127,233

4. According to the third edition HPSO/CNA Pharmacist *Claim Report* analysis, the average total incurred for claims alleging that the wrong dose/strength was dispensed increased how much compared to the Pharmacist Liability *Claim Report*: 2nd edition?
- a. 10%
- b. 22%
- c. 37%
- d. 46%

5. The *Claim Report* found that wrong dose/strength errors are most often associated with
- a. Human errors
- b. Environmental factors, such as workplace distractions and understaffing
- c. Misinterpretation of a prescription, such as pulling the incorrect medication strength from the shelf
- d. All of the above
- e. A and B only

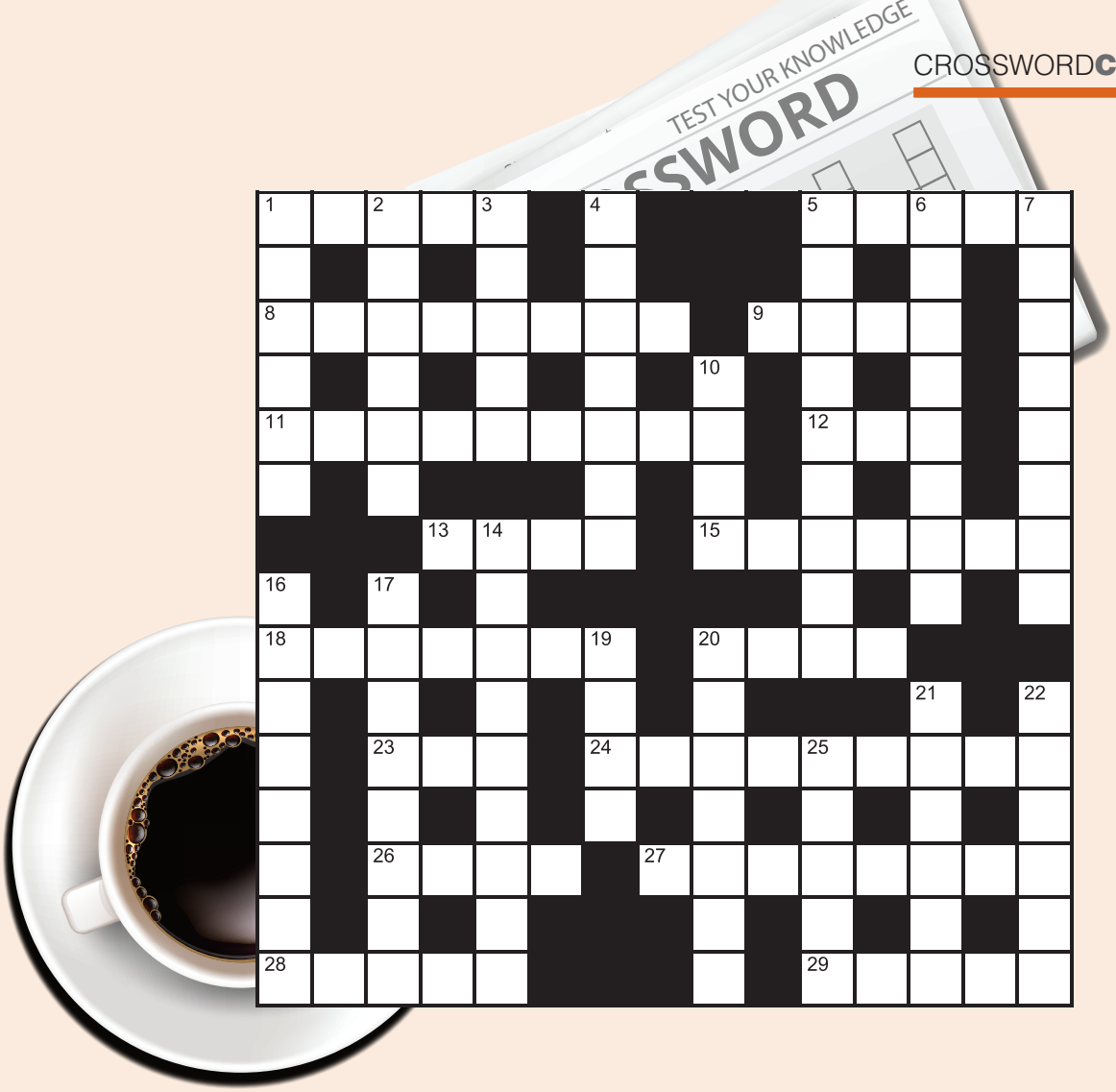
6. Consider these behaviors: transposing the numbers in a medication dose, mishearing a telephone prescription order, or selecting the wrong drug from a drop-down menu. Which behavior associated with medication errors does this best describe?
- a. System failure
- b. Human error
- c. At-risk behavior
- d. Reckless behavior

7. Consider these behaviors: drug diversion, acts of retaliation, working under the influence of alcohol or drugs on the job, or continuing to engage in at-risk behavior despite coaching. How should you best address the behaviors?
- a. Console the individual(s) involved and engage them in training.
- b. Coach the individual(s) involved on the risks associated with their behavior.
- c. Reward the individual(s) involved with empathetic, nonjudgmental, respectful support, because their intentions were good.
- d. Punish the individual(s) involved, taking swift, appropriate disciplinary action according to human resources policies and statutory requirements, as applicable.

8. **During the medication dispensing phase, pharmacies and pharmacists have the opportunity to positively affect, identify, and prevent wrong drug errors by**
   a. Ensuring sufficient staffing levels
   b. Implementing bar code scanning
   c. Offering and conducting patient counseling
   d. All of the above
   e. None of the above

9. **According to ISMP's best practices, all of the following serve as an evidence-based approach to medication error reduction EXCEPT**
   a. Barcode verification technology
   b. Standardized medication reconciliation
   c. Oral methotrexate dose/high-alert medications
   d. Confirm patient identity (ID)
   e. External medication safety resources

10. **With postmedication error actions, and after medical concerns and patient notification are addressed, which is NOT a general risk management step that should be taken?**
    a. Notify appropriate internal personnel (pharmacy manager, supervisor, risk manager, pharmacy owner, or others per the organizational procedure) and the prescriber.
    b. Secure/quarantine any equipment, medications, active ingredients, or supplies involved in the event.
    c. Document the error in the patient profile.
    d. Ignore any threat from the patient of a claim or lawsuit. The situation will eventually go away.
    e. Consider reporting to anonymous voluntary reporting programs to help prevent similar errors from occurring at other organizations.



Across

1 Coffee for those sensitive to caffeine
5 Type of insulin that is absorbed slowly and is long lasting
8 Synthetic opioid that's 100X more potent than morphine
9 Boring or dull
11 Artificial sweetener in the news
12 Type of cell in the eye that detects the size, shape, and brightness of a visual image
13 Beachy vacation spot
15 German measles
18 Potential adverse effect of morphine
20 This kind of wave pattern is a sign of severe hyperkalemia
23 Absolute (abbr.)
24 A substance, accumulates on the surface of a solid
26 Previously used powder that can pose an inhalation risk to infants
27 Tennessee home of the Manhattan Project
28 Track-and-trace regulation
29 Main therapy for Parkinson's disease

Down

1 Pay or subsidize
2 Shade provider
3 Natural aptitude or talent
4 Enzyme that catalyzes the hydrolysis of starch into sugars
5 High levels can result in jaundice
6 Patients should take medications according to a _____
7 Mature bone in which parallel fibers form multiple layers
10 Painful ligament injury
14 Little bit
16 Main site of blood flow regulation within the liver
17 Guitar with no plug
19 0.035 ounce
20 Support or keep going
21 Physical exercise focusing on the heart
22 Groups of related animals or plants
25 Pharmacists in these areas are critical health care providers

Solution is available online at pharmacytoday.org.