There’s no denying that technology has changed the health care industry: From ensuring continued care access during the COVID-19 pandemic via telemedicine to the advent of precision therapies used to treat cancer, it’s difficult to find part of the industry that technology hasn’t touched.

In the pharmacy space, technology-driven improvements have changed medication. In our cover story this month, we look at how augmented intelligence is revolutionizing providers’ abilities to take a predictive and personalized approach—rather than a reactive approach—to disease management. Machine learning algorithms and health care information technology are poised to provide clinical decision support services that will ensure medication safety and contribute to a reduction of harm.

Other developments, such as nanosensor-embedded pills, can help address medication adherence across the therapeutic spectrum. But we would be remiss to laud these advances without examining the potential ethical issues—from patient autonomy to third-party interference—that may stem from such advances.

Elsewhere in this month’s issue, we also look at messenger RNA (mRNA) vaccine technology, which is yet another technological breakthrough that has changed our lives for the better. mRNA became a buzzword in 2020 when the Pfizer-BioNtech and Moderna COVID-19 vaccines entered the public consciousness. Although this particular application of mRNA vaccine technology may be new, the technology has been in development for decades, evidenced by the numerous mRNA vaccines for conditions such as HIV, cancer, and other viruses in various states of preclinical and clinical research. It is our goal to keep you abreast of these advances as they continue to emerge in 2022 and beyond.

As always, thank you for reading.
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Is Automated Prescription Pickup the Future of Pharmacy?

ScriptCenter kiosks are an ATM and an Amazon locker rolled into one. By Lauren Biscaldi

Is automation the future of the pharmacy? According to Sean Slovenski, Asteres chairman, it just might be. Asteres is the company behind ScriptCenter kiosks and lockers, a technology solution that allows for the secure pickup of prescription medications anytime, day or night. Slovenski chatted with Drug Topics® in a recent episode of Inside the Practice, where he discussed the importance of accessibility in health care.

Drug Topics®: How have your experiences driven the work you do today with Asteres? Are there any gaps in the industry?

Sean Slovenski: Part of the issue with most things in health care is affordability and access. There are a thousand other things that go around it, but access and affordability tend to be the biggest barriers.

In essence, we bring these prescription ATMs to remote locations—[like] out in the military, rural settings...even at grocery stores and places like that—that need extra support because either their pharmacies are not open as long as they used to be prepandemic, or, in some cases, many pharmacies and retail locations have closed because they couldn’t find workers to keep them open.

Having access to your medication is primary to keep your health where it needs to go, whether it’s behavioral health–related medications or physical health–related medications. That’s the interesting thing—we can mail stuff to people's homes, and that’s a great option, but people like to go out. Having a pickup destination where you can get your prescription filled, then heading on to the rest of your day, is quite convenient for people.

Drug Topics®: Can you explain what the ScriptCenter kiosk is and how it works?

Slovenski: The simplest way to understand it is with 2 analogies. We've all used ATM machines. I'm showing my age...Back in the '80s and '90s, that was a weird thing. Banks [would say], “No one's ever going to use that because they want to come to the bank.” Now who goes to a bank anymore? [ScriptCenter] works the same way. Different laws in different states decide how you can dispense medications and the process of doing that, but essentially, ScriptCenter is an ATM. Instead of spitting out dollar bills, it will spit out your prescription...at a pickup location.

The other [analogy] is more like an Amazon locker system, where your prescription would be delivered to a locker within a bank of lockers at a store or community center. And just like picking up a package at an apartment complex, you get a little code, type in your name, and it verifies you through face recognition or a code that you have and, hey, locker 32A, there's your penicillin for you today, or here's your blood pressure medicine, and the locker opens for you. So it's an ATM and an Amazon locker combined into one.
Cost, Culture Affect Access to Autoimmune Disease Care

Pharmacists are well positioned to address the care issues faced by patients living with autoimmune diseases. By Frieda Wiley, PharmD

Estimates regarding the prevalence of people with autoimmune conditions range from as few as 24 million people to nearly 50 million people across the United States. Scientists have identified more than 80 autoimmune diseases, running the gamut of conditions from type 1 diabetes and rheumatoid arthritis to scleroderma and multiple sclerosis. Despite their collective commonalities, many patients with autoimmune conditions—many of which fall under the umbrella of rare diseases—face access barriers, with health insurers and pharmacy benefit managers bearing the brunt of blame.

Although industry experts agree cost is a huge barrier to treatment, views on whether this is the greatest challenge faced by patients with autoimmune diseases vary and are sometimes in opposition. However, all agree that pharmacists can have a tremendous impact in helping patients access their medications.

For Denise Summers, PharmD, BCGP, CDCES, rare disease advocate and geriatric clinical pharmacist at Landmark Health in Boston, Massachusetts, the wounds caused by financial burdens cut much deeper than the pocketbook. “One of the greatest hurdles those with rare autoimmune conditions face is continuity of care,” Summers told Drug Topics.

Interruption of care is a topic Pam Cusick, senior vice president of Rare Patient Voice in Annapolis, Maryland, knows all too well both on a personal and professional level. She shared the story of a situation where a child with Crohn disease changed jobs, resulting in an insurance mix-up. The child needed an infusion but was denied treatment until her parents paid the $24,000 fee via credit card. “They got their money back, but it was a terrible experience,” Cusick said.

Cusick believes pharmacists are well positioned to help patients tackle this and other access-related issues. Pharmacists are often well versed in navigating the intricacies of the payer world. This experience allows them to educate patients and their families about cost-saving measures. Pharmacists can also leverage their rapport as highly influential and trustworthy health care professionals. “There is so much information out there, and they need a good resource they can trust,” Cusick said.

Engaging with a trustworthy health care provider can also help address the coverage gaps frequently exacerbated by racial, cultural, and ethnic divides. Summers pointed out that patients who are either underinsured face the substantial risk of failing treatment, as they often engage in behaviors such as reducing medication use due to costs. Nonetheless, people of color, regardless of race or ethnicity, are less likely to have health insurance than White patients, according to a 2019 report conducted by the Kaiser Family Foundation.

“There is still mistrust of the medical community,” Cusick said. “There are cultural differences pharmacists should be aware of so they can meet people where they are and help patients feel comfortable.” The differences to which Cusick referred transcend medical mistrust owing to painful history of institutional racism plaguing communities of color. Cultural beliefs, creeds, and norms can also influence outcomes. In some cultures, having an illness such as an autoimmune disease or cancer may be seen as a weakness, meaning that people from those cultures may be less likely to seek medical help.

Cusick believes pharmacists can intervene in these kinds of cases, easing the patient’s anxiety and answering questions they might find uncomfortable otherwise. “The biggest hurdle patients with autoimmune conditions face is connecting with others who have had their lived experience,” Cusick said. “It can be very isolating.”

For references, visit drugtopics.com.

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VACCINES

mRNA Technology Leads to Advances in HIV Vaccine Candidate

Results of a recent preclinical study provide proof of concept that an mRNA HIV vaccine is safe, immunogenic, and induces CD4–T-cell responses. By Kmeone Kingdom, MPH, PharmD candidate

Messenger RNA (mRNA) vaccines have made a remarkable impact on the trajectory of the COVID-19 pandemic. The success of these vaccines raises the question of whether this technology can be used to tackle the more complex task of creating a vaccine to fight HIV.

Nearly 37.7 million people were living with HIV in 2020 and 680,000 people died because of related illnesses, according to statistics provided by the United Nations Programme on HIV/AIDS.1 In 2020, during the height of the COVID-19 pandemic, the Global Fund to Fight AIDS, Tuberculosis, and Malaria reported a 41% decrease in HIV testing and a 37% decrease in the diagnosis and treatment of HIV/AIDS across 32 countries in Africa and Asia.2 It is clear more effort is needed to make an impact on the ever-growing HIV epidemic.

mRNA vaccines may be 1 piece of this expanded effort. They are, according to Nature Medicine,3 a “uniquely positioned” technology. At Moderna, 2 mRNA HIV vaccines are being developed. The first, mRNA-1644, is being created in conjunction with the International AIDS Vaccine Initiative and the Bill and Melinda Gates Foundation. The second, mRNA-1574, is being evaluated in collaboration with the National Institutes of Health. In late January, Moderna announced the first patient in the mRNA-1644 phase 1 clinical trial (NCT05001373) was dosed.4

A recent study, also published in Nature Medicine,5 led by Paolo Lusso, MD, PhD, of the National Institute of Allergy and Infectious Diseases, sought to determine whether mRNA-expressing membrane-anchored HIV-1 envelopes (Env) and simian immunodeficiency virus Gag proteins can generate virus-like particles that induce antibodies that neutralize and reduce infection in monkeys and mice. This preclinical study evaluated a multiclade HIV-1 env-gag mRNA vaccine in animal models, where the vaccine’s efficacy was evaluated based on time to infection over a 13-week period of low-dose vaccine administration.

This same technology used to create the COVID-19 vaccines showed positive results in monkeys and mice. Instead of targeting the SARS-CoV-2 spike protein, the vaccine targets 2 essential HIV proteins, Env and Gag. The study results showed vaccinated animals had a 79% risk reduction per vaccine exposure. In the studied mice, Lusso and colleagues reported the Env proteins greatly resembled those in the entire virus. Among the monkeys, 2 of the 7 subjects remained unaffected after the 13-week inoculation schedule, suggesting the virus-particle mRNA platform is a capable approach for the development of an HIV vaccine.

Although the results suggested benefits, the authors acknowledged some study limitations. First, the neutralization titers to combat the virus did not reach optimal levels that have been reported by other studies as protective in the body. Only 2 animals were fully protected by the vaccine. However, the particular strain investigators were trying to neutralize was challenging, and the vaccine still induced a 79% risk reduction per exposure. Finally, this vaccine has been tested in only 1 study, and more studies should be done to confirm these findings.

mRNA technology may be the right platform to develop vaccines for different disease states, but more studies must be done. The study by Zhang et al provided more information on the positives this technology presents. It proved this vaccine is safe, immunogenic, and can induce CD4 T-cell responses in animals—and potentially in humans.6

Check out the next page for the latest on some of the mRNA vaccines in development.

For references, visit drugtopics.com.

Kmeone Kingdom, MPH, is currently a PharmD candidate at the South College School of Pharmacy, anticipated to graduate in spring 2022. This article was created during a virtual advanced pharmacy practice experiential rotation at STACK.

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mRNA Vaccine Technology Update

Moderna, Pfizer, and Boehringer Ingelheim are among the pharmaceutical companies investigating the applicability of mRNA vaccines to treat and prevent other conditions. In addition to a vaccine for HIV, mRNA is being explored as a potential vehicle to create vaccines for several other conditions.1

Influenza
A messenger RNA (mRNA) influenza vaccine has the potential to improve on the current flu vaccine paradigm. Three mRNA flu vaccines began phase 1 clinical trials in 2020.

Together, Sanofi and Translate Biologics are investigating a monovalent vaccine candidate for the hemagglutinin protein of the A/H3N2 strain of the influenza virus.2 When the A/H3N2 strain is most dominant, flu activity may be more severe, particularly among at-risk groups, such as older adults and younger children.

Pfizer’s phase 1 trial (NCT05052697)3 is evaluating the response to their mRNA flu vaccine in a group of healthy adults between 65 and 85 years across the United States. Participants will randomly receive 1 of 4 dose levels of the company’s monovalent vaccine candidate (A or B strain of the virus), 1 of 4 dose levels of the bivalent candidate (A and B strains of the virus), the quadrivalent candidate, or a currently approved quadrivalent flu vaccine.

In July 2020, Moderna announced the dosing of the first participants in a phase 1/2 study of mRNA-1010, a quadrivalent flu vaccine candidate,4 to evaluate the safety and immunogenicity of 3 levels of doses of the vaccine targeting hemagglutinin surface proteins from 4 World Health Organization–recommended influenza strains. Moderna is also investigating an mRNA candidate (mRNA-1073) combining vaccines for COVID-19 and the flu.

Respiratory Syncytial Virus
Previous investigations into a vaccine for respiratory syncytial virus (RSV) have been unsuccessful, with early candidates ultimately strengthening rather than protecting against the disease.5 Currently, no vaccine against RSV exists.

Modern is now studying mRNA-3145,6 an RSV vaccine candidate that uses the same lipid nanoparticle as their COVID-19 vaccine. In late 2021, the company announced interim data7 from a phase 1 trial (NCT04528719) evaluating the tolerability and reactogenicity of mRNA-1345 in groups of participants between 18 and 49 years, 65 and 79 years, and 12 and 59 months. Results showed that at 1-month post vaccination, 50-µg and 100-µg doses were “generally well tolerated” in the study’s cohort of younger adults. Moderna expects the study to be completed in 2023.

Cytomegalovirus
Modern’s cytomegalovirus (CMV) vaccine candidate, mRNA-1647, combines 6 mRNAs into 1 vaccine aimed at protecting against CMV—a significant unmet need, according to a company press release. CDC estimates suggest 1 in 200 babies are born with CMV, 1 of 5 of whom will experience “devastating sequelae,” such as hearing loss, seizures, and blindness, as well as potential complications later in life.9

The phase 3 CMVictory study (NCT05085366) will evaluate safety and efficacy of mRNA-1647 against primary CMV infection in women between 16 and 40 years. Investigators are aiming to enroll 8000 participants (6900 of childbearing age) across 150 global sites.

Epstein-Barr Virus
In January 2022, Moderna announced10 the dosing of the first candidate in the company’s phase 1 Eclipse study (NCT0164094) of mRNA-1189, an Epstein-Barr virus (EBV) vaccine candidate. Although EBV—which causes infectious mononucleosis—affects “millions of adolescents globally,” there is no vaccine currently available.

The goal of mRNA-1189 is to prevent EBV-induced infectious mononucleosis and potentially EBV infection itself. The vaccine contains 4 mRNAs that encode EBV envelope glycoproteins gH, gL, gp42, and gp220.

Cancer
Cancer vaccines are currently being studied both alone and in combination with chemotherapy and immunotherapy. Some of these vaccines are personalized—created for individual patients based on their tumor samples—whereas others target the proteins found in cancer cells more globally.11

BioNTech and Regeneron Pharmaceuticals are currently collaborating on an mRNA cancer vaccine for advanced melanoma.12 The vaccine, BNT111, is currently in a phase 2 clinical trial (NCT04526899). In late 2021, BioNTech was granted an FDA fast track designation based on “available preclinical and clinical data showing the potential of BNT111 to overcome current limitations in the treatment of inoperable therapy-resistant advanced-stage melanoma,” according to a press release.13

BioNTech is also collaborating with investigators at the University Medical Center Groningen in the Netherlands in the phase 1 OLIVIA clinical trial (NCT04163094)14 to evaluate the W_ova1 mRNA vaccine in combination with neoadjuvant chemotherapy for ovarian cancer. The first-in-human study is estimated to be completed in late 2023.

Boehringer Ingelheim, CureVac, and Ludwig Cancer Research have joined forces to study mRNA vaccine BI 1361849 (CV9202), a self-adjuvanting mRNA-based immunotherapeutic cancer vaccine to “mobilize the immune system” to fight tumors.15 It contains 6 mRNAs coded for 6 different antigens commonly expressed in non–small cell lung cancer (NSCLC).16 It is being investigated in a phase 1/2 clinical trial (NCT03164772)16 as a combination treatment with durvalumab or durvalumab plus tremelimumab for NSCLC.

Moderna is studying at least 3 mRNA vaccines for cancer in clinical trials, 2 of which are personalized. KEYNOTE-942 (NCT03897881) is studying mRNA-4157 as an adjuvant therapy to pembrolizumab in patients with high-risk melanoma.17 KEYNOTE-603 (NCT03313778) is studying the safety, tolerability, and immunogenicity of mRNA-4157 in patients with solid tumors, both alone in those with resected solid tumors and in combination with pembrolizumab in those with unresectable solid tumors.18

A third Moderna vaccine—mRNA-5671/V941—is in a phase 1 study (NCT03948763)19 as both a monotherapy and in combination with pembrolizumab to target a specific cancer cell protein found in NSCLC, colorectal cancer, and pancreatic cancer.20

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IMPORTANT SAFETY INFORMATION

• VASCEPA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to VASCEPA or any of its components.

• VASCEPA was associated with an increased risk (3% vs 2%) of atrial fibrillation or atrial flutter requiring hospitalization in a double-blind, placebo-controlled trial. The incidence of atrial fibrillation was greater in patients with a previous history of atrial fibrillation or atrial flutter.

• It is not known whether patients with allergies to fish and/or shellfish are at an increased risk of an allergic reaction to VASCEPA. Patients with such allergies should discontinue VASCEPA if any reactions occur.

The wholesale price of VASCEPA is $344.22 for 120 1g capsules and $402.73 for 240 0.5g capsules. Commercially insured patients can save with the VASCEPA Savings Card. VASCEPA Savings Card may not be used to obtain prescription drugs paid in part by some Federal or State Programs, or where prohibited by law; see vascepahcp.com for more information. Generic icosapent ethyl capsules available from Hikma Pharmaceuticals do not have an approved indication for cardiovascular risk reduction. Amarin retains exclusivity for cardiovascular risk reduction and the Hikma generic should not be dispensed for this indication.

With the rise of COVID-19 cases nationwide, the Office for Civil Rights (OCR) has temporarily lifted penalties associated with private telehealth communications between health care providers and their patients. For additional information, please visit the temporarily updated guidelines at hhs.gov/hpaa.
IMPORTANT SAFETY INFORMATION (cont’d)

- VASCEPA was associated with an increased risk (12% vs 10%) of bleeding in a double-blind, placebo-controlled trial. The incidence of bleeding was greater in patients receiving concomitant antithrombotic medications, such as aspirin, clopidogrel or warfarin.
- Common adverse reactions in the cardiovascular outcomes trial (incidence ≥3% and ≥1% more frequent than placebo): musculoskeletal pain (4% vs 3%), peripheral edema (7% vs 5%), constipation (5% vs 4%), gout (4% vs 3%) and atrial fibrillation (5% vs 4%).
- Common adverse reactions in the hypertriglyceridemia trials (incidence ≥1% more frequent than placebo): arthralgia (2% vs 1%) and oropharyngeal pain (1% vs 0.3%).
- Adverse Events, Product Complaints, or Special Situations may be reported by contacting AmarinConnect at 1-855-VASCEPA, emailing AmarinConnect@AmarinCorp.com, or calling the FDA at 1-800-FDA-1088.
- Patients receiving VASCEPA and concomitant anticoagulants and/or anti-platelet agents should be monitored for bleeding.

Please see adjacent Brief Summary of full Prescribing Information for VASCEPA or go to www.vascepahcp.com.

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1Cardiovascular events including myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization.

2.2 Dosage and Administration

The daily dose of VASCEPA is 4 grams per day taken as either:
- Four 1 gram capsules twice daily with food.
- Two 2 gram capsules once daily with food.

Avoid patients to swallow VASCEPA capsules whole. Do not break open, crush, dissolve, or chew VASCEPA.

3. DOSAGE FORMS AND STRENGTHS

VASCEPA capsules are supplied as:
- 0.5 gram amber-colored, oval, soft-gelatin capsules imprinted with VASCEPA
- 1 gram amber-colored, oblong, soft-gelatin capsules imprinted with VASCEPA

4. CONTRAINDICATIONS

VASCEPA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to VASCEPA or any of its components.

5. WARNINGS AND PRECAUTIONS

5.1 Atrial Fibrillation/Flutter

VASCEPA is associated with an increased risk of atrial fibrillation or atrial flutter requiring hospitalization. In a double-blind, placebo-controlled trial of 8,178 statin-treated subjects with established cardiovascular disease (CVD) or diabetes plus an additional risk factor for CVD, adjudicated atrial fibrillation or atrial flutter requiring hospitalization for 24 or more hours occurred in 217 (3%) patients treated with VASCEPA compared with 84 (2%) patients receiving placebo [HR= 1.5 (95% CI 1.14, 1.98)]. The incidence of atrial fibrillation was greater in patients with a previous history of atrial fibrillation or atrial flutter.

5.2 Potential for Allergic Reactions in Patients with Fish Allergy

VASCEPA contains ethyl esters of the omega-3 fatty acid, eicosapentaenoic acid (EPA), obtained from the oil of fish. It is not known whether patients with allergies to fish and/or shellfish are at an increased risk of an allergic reaction to VASCEPA. Inform patients with known hypersensitivity to fish and/or shellfish about the potential for allergic reactions to VASCEPA and advise them to discontinue VASCEPA and seek medical attention if any reactions occur.

5.3 Bleeding

VASCEPA is associated with an increased risk of bleeding. In a double-blind, placebo-controlled cardiovascular outcomes trial of 8,179 patients, 482 (7%) patients receiving VASCEPA experienced a bleeding event compared to 340 (5%) patients receiving placebo. Serious bleeding events occurred in 111 (3%) of patients on VASCEPA vs. 85 (2%) of patients receiving placebo. The incidence of bleeding was greater in patients receiving concomitant antithrombotic medications, such as aspirin, clopidogrel, or warfarin.

6. ADVERSE REACTIONS

The following adverse reactions are described below and elsewhere in the labeling:
- Atrial Fibrillation or Atrial Flutter [see Warnings and Precautions (5.1)]
- Potential for Allergic Reactions in Patients with Fish Allergy [see Warnings and Precautions (5.2)]
- Bleeding [see Warnings and Precautions (5.3)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Cardiovascular Outcomes Trial

In a double-blind, randomized, placebo-controlled cardiovascular outcomes trial, 8,178 statin-stabilized patients were randomized to receive VASCEPA or placebo and followed for a median of 4.9 years [see Clinical Studies (14.1)]. The median age at baseline was 64 years, 29% were women, 90% White, 5% Asian, 2% were Black, and 4% identified as Hispanic ethnicity.

Common adverse reactions (incidence ≥3% in VASCEPA and ≥1% more frequent than placebo) included musculoskeletal pain, peripheral edema, constipation, cough, and atrial fibrillation.

Hemorrhagic/Neurologic Trials

In two randomized, double-blind, placebo-controlled trials in patients with triglyceride levels between 200 and 2000 mg/dL for treated 12 weeks, adverse reactions reported with VASCEPA at an incidence ≥1% more frequent than placebo based on pooled data included arthralgia and arthralgic pain.

6.2 Postmarketing Experience

Additional adverse reactions have been identified during post-approval use of VASCEPA. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Diarrhea
- Blood triglycerides increased
- Abdominal discomfort
- Pain in the extremities

7. DRUG INTERACTIONS

7.1 Increased Bleeding Risk with Anticoagulants and Antiplatelet Agents

Some published studies with omega-3 fatty acids have demonstrated prolongation of bleeding time. The prolongation of bleeding time reported in those studies has not exceeded normal limits and did not produce clinically significant bleeding episodes. Multiple patients receiving VASCEPA and concomitant anticoagulants and/or antiplatelet agents for bleeding.
Counseling Pearls: Allergic Asthma Treatment

Allergic asthma can be a complicated and confusing diagnosis. By Keith Loria

When it comes to treating allergic asthma, “the pharmacist is in the ideal position to ensure the patient understands their condition, how to avoid triggers, how to manage an attack, and how medications work,” Kashmira Govind, a pharmacist for the Farr Institute, explained. “This is especially important for [patients with] newly diagnosed asthma. It is a complicated and confusing diagnosis.”

Troy J. Smith, PharmD, assistant professor of pharmacy practice at William Carey University School of Pharmacy in Biloxi, Mississippi, noted that allergen avoidance is still the best approach, combined with being prepared for those times when exposure to allergens or triggers is unavoidable. “If someone were allergic to cut grass but needed to mow the lawn, I’d tell [them] to wear a mask, possibly premedicate with a newer-generation antihistamine, and to have their rescue inhaler nearby,” Smith said. “And, of course, be [adherent] with their long-acting inhaler.”

Pharmacists must also counsel patients to ensure they are doing things correctly. “This is especially important for [older adults] and children—those with limited hand mobility,” Govind said. “The patient can practice the use of an inhaler in the presence of the pharmacist, who can patiently instruct them correctly.”

Pharmacists involved in medication therapy management can conduct interviews, asking a series of questions and assessing the patient’s level of control. “If adherence is there and the patient still suffers, the pharmacist may recommend a step up in therapy,” Smith said. “If the [asthma] is well controlled, then usually nothing needs to be done. However, be attentive to the steroid dose and see [whether] it can be lowered.”

Pharmacists can also help by checking medication ingredients to determine whether they contain any known allergen. And, pharmacists can suggest cost-effective steps to reduce triggers in the home, recommending a dust mite-proof mattress and pillow covers, dehumidifiers, nontoxic pest control, and air filters.

Researchers are currently evaluating mepolizumab (Nucala), a new drug that can treat the cause of asthma rather than the symptoms. “[Mepolizumab] switches off the cascade reaction of inflammation that causes an asthma attack,” Govind said. It is a biologic injectable that inhibits IL-5 to decrease the number of asthma attacks.

Recent recommendations from the Global Initiative for Asthma (GINA) have been to use budesonide/formoterol fumarate dihydrate (Symbicort) as a reliever, as opposed to short-acting β-agonists (SABAs). “The idea is that [budesonide/formoterol fumarate dihydrate] can provide suitably quick relief of symptoms without causing the patient to become overly reliant on the SABA, leading to airway remodeling,” Smith said. “Future editions of GINA will examine the use of [budesonide/formoterol fumarate dihydrate] as a reliever more closely. The challenge will be to persuade patients to try something different from the SABA, which has worked for them very quickly their entire lives.”

Recent small trials have compared benralizumab (Fasenra) with mepolizumab to treat eosinophilic asthma. Although initial eosinophil reductions were initially similar, benralizumab, Smith explained, seems to have kept more patients at a lower eosinophil count for a longer time. Currently, benralizumab is approved in the United States as an adjunctive therapy for eosinophilic asthma for patients 12 years and older.

For references, visit drugtopics.com.
From smart pills to augmented intelligence, technology has presented the health care industry with a host of options to improve medication adherence and safety.
Novel computer technologies for improving medication adherence and safety have ushered in a new era of medication reminder and tracking apps, smart pill canisters, and medications with nanosized biosensors contained within. Although these technologies represent new treatment paradigms for a variety of diseases, they could have unintended implications.

By John Schieszer

ntipsychotics—available as oral disintegrating tablets, oral solutions, short-acting intramuscular injections, and long-acting injectable formulations—are now being combined with wireless technology. Tahir Rahman, MD, an associate professor of psychiatry at Washington University School of Medicine in St Louis, Missouri, explained how one approach includes a patch worn on the abdomen to track and record medication adherence. A related smartphone app tracks medication ingestion and activity level data, as well as self-reported mood and other factors.

“I see trackable pills playing an important role in the future. People who are adherent with care don’t really need them, but there are always medications that are difficult to adhere to,” Rahman told Drug Topics®. These medications include those that require dosing 3 or 4 times a day. “That is where some apps can be helpful to increase adherence.”

Advances in Medication Tech

With wireless technologies, patients can share their collected data with others, including their health care provider. Aripiprazole tablets with sensors and other similar products are being touted as electronic drugs, nanodrugs, or digital drugs, Rahman explained. A recently published review on emerging smart technology innovations in the health care sector suggests various advanced technologies and methods may now significantly improve medication adherence. Two significant advances have been the ability to measure medication adherence and safety issues with medication event monitoring systems (MEMS) and smart blister packs containing radio frequency identification technology.

MEMS is a “customizable medication package” capable of recording and storing 4000 dosing events, according to a review published in the Global Health Journal. Microcircuits record each date and time when the packaging is opened on either the SmartCap or TrackCap product.

The ID-Cap System—another smart medication adherence tool,
manufactured by etectRx—includes an ingestible sensor that provides real-time dose-level ingestion event verification. According to Eric Buffkin, etectRx president and CEO, the ID-Cap System is currently the only FDA-cleared method to document a dosing event, going beyond reminders and self-reporting. “In addition to the ease of patient use, the ID-Cap System’s real strengths are in the verification of ingestion and thorough reporting and tracking of adherence,” Buffkin said. In this new era of applied technology, partnerships between pharmacists and software developers are becoming more commonplace in order to maximize medication outcomes and improve overall safety. Pharmacists, Buffkin said, are uniquely positioned to leverage this technology to improve medication safety. “As medications increase in expense and complexity, pharmacists can provide even more value (by) ensuring medications are taken as prescribed, and etectRx would welcome the opportunity to partner with pharmacy further on this initiative,” he added.

"SMART" THERAPEUTICS CREATE ETHICAL CONUNDRUMS

Technology can be exciting, and technological advances in the health care industry have certainly made waves. However, with each of these new advances comes a set of potential downsides and a myriad of ethical dilemmas that must be addressed. Drug Topics® spoke with Craig M. Klugman, PhD, Vincent de Paul Professor of Bioethics in the Department of Health Sciences at DePaul University College of Science and Health in Chicago, Illinois, to discuss some of the bioethical dilemmas associated with "smart" medications today.

Drug Topics®: What are some of the biggest ethical issues associated with smart medications and digital therapeutics?

Klugman: Privacy is the biggest issue, including control over your data, who can view the data, and being tracked. [Although] health care providers and hospitals are bound by the Health Insurance Portability and Accountability Act (HIPAA), device manufacturers, programmers, and insurers are not. (However), they will have access to the same information.

[Other issues include] informed consent for a product that can constantly be changing (ie, updates and new user agreements) and coercion. A health insurer, provider, or hospital system may encourage patients to take a digital solution because they can be tracked. Maybe an insurance company will not pay for a medication if they learn the patient is not taking it as prescribed. Informed consent would cover the medical treatment, but digital solutions may require software and hardware, and those are covered by user agreements that can be very long, complicated, and hard to understand. [which is] the opposite of what an informed consent document should be.

How can providers ensure patients are providing fully informed consent before prescribing digital therapeutics?

Klugman: Many question whether truly fully informed consent is possible. Informed consent consists of helping patients to understand the risks, benefits, processes, and alternatives, but it’s not every risk. It’s only risks that may apply to that person, or risks that are statistically more common. The problem with digital therapeutics is that we layer a user agreement on top of informed consent. Informed consent exists to protect the patient. These documents and conversations use everyday language and explain to patients their rights. [However], a user agreement is usually long, written in legalese, and is intended to protect the company’s rights. It is also possible that these approaches are at odds. For example, informed consent is all about process, asking questions, and even allowing a person to change their mind. A user agreement is about limits, protecting the company’s intellectual property, and often limiting how people can respond to problems with the product, (such as arbitration clauses). Also, if a patient does not agree with something in a user agreement, they may still have to agree to get needed treatment—or they [must] forgo getting medical treatment.

Insurance providers and other payers are already quite involved in health care decision-making. Do you think the advent of these trackable smart medication technologies has the potential to increase that involvement?

Klugman: Smart medication technologies will absolutely increase insurer involvement in medical decision-making and at the individual patient level. With the feedback these technologies provide, an insurer could say, “We don’t think this drug or device is having the intended effect, so we won’t cover it any longer,” even though the patient and their provider might think it is working. A patient might get a text from their insurer that they forgot to take their pill, and unless they take it as prescribed, [the insurer] won’t cover it.

Insurance companies are used to making decisions based on population-level data analysis, but now they can make decisions based on the individual’s data. Given how used we are to giving up our private information to technology companies, most people probably won’t think twice about giving up more information to their insurer. HIPAA only protects data with a patient’s health insurer.

To read the full interview with Klugman, visit drugtopics.com.
Medication Safety 2.0 / Cover Story

Augmented Intelligence and Personalized Medicine

The current technological revolution is paving the way for health care providers to make the move from reactive disease management to a predictive and personalized approach. “I think we are in an era of digital health, where we can use wearables, telehealth, digital therapeutics, and health information technology (HIT) to improve medication safety,” said Sandra L. Kane-Gill, PharmD, MSc, a critical care medication safety officer in the Department of Pharmacy at the University of Pittsburgh Medical Center in Pennsylvania.

Kane-Gill refers to this technology as augmented—not artificial—intelligence. The volume of data health care professionals can access for a single patient continues to increase, and augmented intelligence can quickly digest that information in an organized manner.

“Augmented intelligence [is the preferred term] because we are designing [HIT] to support health care professionals’ decisions,” Kane-Gill said. “The [biggest] advantage to augmented intelligence is the support it provides by managing large amounts of data with a streamlined process, typically [faster] than humans.”

It may be possible to lower morbidity and mortality across a variety of conditions by using validated augmented intelligence algorithms. Rahman believes machine learning will allow providers to spot medication safety issues much earlier than is currently possible. “Machine learning is the future. We can use big databases, and we will know which patients do better on certain drugs,” Rahman said.

The Game Is Just Beginning

Kane-Gill and her team are working to develop machine learning algorithms that can be used to improve drug-related acute kidney injury detection and prevention. Currently, HIT can provide clinical decision support to aid with medication safety. However, HIT has the potential to do much more than pick up on potential drug safety issues. “I think we have moved beyond the first inning,” Kane-Gill said.

The COVID-19 pandemic has expedited patient monitoring through telemedicine. Now new transmitting devices may help to maintain effective and sustainable communication. The use of wearables for medication monitoring is increasing and these wearables can handle a huge volume of data and provide real-time responses. “We are not sure when medication monitoring will reach the ninth inning, as we are just beginning to understand multiracial, multiethnic, and genetic-specific research and technology [needed] to guide advanced therapies,” Kane-Gill said.

Daniel C. Malone, PhD, BSPharm, professor in the Department of Pharmacotherapy at the University of Utah College of Pharmacy in Salt Lake City, said that although medication adherence continues to be an issue, there is not a one-size-fits-all approach. In fact, Malone questions whether patients will be willing to consent to having someone look over their shoulder to observe their medication-taking behavior.

Machine learning, which can detect unique patterns of use associated with a greater risk of negative health outcomes, is useful for generating hypotheses and perhaps identifying some previously undiscovered characteristics. “On the other hand, I don’t see it fitting into the daily practice of pharmacy in a significant manner,” Malone said. “Perhaps some nuggets of gold will come from the approach, but I think those will be relatively rare and less impactful than many anticipate.”

Lisa Schwartz, PharmD, senior director of professional affairs at the National Community Pharmacists Association, said it is exciting to see how advances in technology are providing patients and their care teams with more objective data to assess drug safety and effectiveness. However, she worries soft skills, such as motivational interviewing, may be pushed to the side and patients will lose some continuity of care. “Pharmacists will still make observations and elicit information that helps treat the patient and not just their data,” Schwartz said. ■

What do you think about the role of technology in medication safety? Share your thoughts and email your comments to lbiscaldi@mjhlifesciences.com.

REFERENCE

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Managing Chronic Kidney Disease in Patients With Diabetes

How can pharmacists help slow the progression of diabetic kidney disease?  By Tzipora R. Lieder, RPh

As of 2019, more than 37 million Americans—11.3% of the population—had diabetes, according to the American Diabetes Association.1 Diabetes is a major risk factor for chronic kidney disease (CKD), a condition with which approximately 1 in 3 adults with diabetes—type 1 (T1D) or type 2 (T2D)—is living.2,3 Many of these patients may progress to end-stage kidney disease (ESKD), requiring dialysis or transplantation.4 Although the progression of CKD can be slowed or even reversed by appropriate drug therapy and lifestyle changes, many patients do not get the treatment they need. In fact, many patients may not receive a diagnosis, as early-stage CKD is asymptomatic.

Wendy L. St. Peter, PharmD, professor at the University of Minnesota College of Pharmacy and an investigator with the United States Renal Data System, is leading a national initiative to advance kidney health through optimal medication management, including incorporating pharmacists into team-based care. “Primary care physicians, where a lot of these patients are being seen for their diabetes or high blood pressure, may not have the time or expertise to manage all these new medications for the purpose of reducing progression of kidney disease,” St. Peter said. Coupled with a shortage of nephrologists, this creates an ideal opportunity for clinical pharmacists with advanced training to work with an interdisciplinary team and manage medication use in diabetic kidney disease (DKD).

As frontline health care workers who know patients, their diagnoses, and their prescriptions well, community pharmacists can be instrumental in the identification and appropriate treatment of DKD, said St. Peter. Urine screening can be valuable in identifying albuminuria (Table 1),5 which is often one of the first signs of CKD, whereas regular blood work is needed to detect declines in estimated glomerular filtration rate (eGFR).

“\[We\ can\ give\ all\ these\ medications\ to\ patients,\ but\ unless\ they\ take\ them,\ they\ don’t\ work.\]”  Candis M. Morello, PharmD, APH, CDECS, FCSHP, FASHP, Director, Diabetes Intense Medical Management Clinic, Veterans Affairs San Diego Healthcare System, California

Double-Duty Drugs
Two recent clinical trials—CREDENCE (NCT02065791) and Dapa-CKD (NCT03036150)—have represented important developments in demonstrating the beneficial renal and cardiovascular effects of sodium-glucose cotransporter 2 (SGLT2) inhibitors, which were initially approved for T2D. “This has really changed our practice and treatment options for patients (who) have CKD and diabetes with albuminuria,” said Abby Hines, PharmD, an ambulatory care clinical pharmacist in the Division of Nephrology, Bone and Mineral Metabolism at UK HealthCare in Lexington, Kentucky.

The Kidney Disease: Improving Global Outcomes (KDIGO) 2020 Clinical Practice Guideline6 for the management of CKD in diabetes recommends SGLT2 inhibitors with metformin as first-line antidiabetic therapy for patients with T2D and CKD. Metformin can be initiated as long as the patient’s eGFR is 30 mL/min/1.73 m² or greater but must be discontinued if the eGFR drops below that (Table 2).7 For patients with T1D, there is no strong evidence for the use of SGLT2 inhibitors, which carry a risk of euglycemic
diabetic ketoacidosis, Hines said.

KDIGO guidelines also recommend patients with diabetes, albuminuria, and hypertension be treated with the highest-tolerated dose of angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker to reduce decline in kidney function. For patients with diabetes and CKD who are not meeting personalized glycated hemoglobin A_{1c} goals, despite being prescribed maximal doses of metformin and SGLT2 inhibitors, KDIGO guidelines recommend adding a glucagon-like peptide 1 receptor agonist (GLP-1 RA). There is ongoing research on the benefits of GLP-1 RAs in CKD that appears promising, Hines said.

An even more recent development that is not included in the most recent KDIGO guidelines is the July 2021 FDA approval of finerenone (Kerendia), a first-in-class nonsteroidal selective mineralocorticoid antagonist shown to reduce risk of serious kidney and heart complications in adults with CKD and T2D. Hines expects to see finerenone used more frequently in the coming months and years.

Lightening the Pill Burden

Because patients with DKD often have other comorbidities, they usually have very complex drug regimens that may feel overwhelming. “We can give all these medications to patients, but unless they take them, they don’t work,” said Candis M. Morello, PharmD, APH, CDGES, FCPS, FASHP, a clinical pharmacist specialist and director of the Diabetes Intensive Medical Management Clinic at the Veterans Affairs San Diego Healthcare System in California. Pharmacists can play a crucial role in reducing the number of prescribed drugs, tailoring regimens, and accounting for lifestyle, cultural beliefs, and medication preferences, from how frequently medications should be taken to decisions on oral vs injectable drugs and the size of ingestible tablets or capsules. Patients often appreciate taking a combination SGLT2 inhibitor with metformin, which reduces the daily pill count, Morello noted.

St. Peter stressed the importance of patient education. “Pharmacists can work with patients to [explain] why they are taking these medications, why they’re important, [and] why these medications can avert future disasters, [such as] ESKD,” she said. Awareness of racial disparities in kidney risk is also imperative, St. Peter noted. African American individuals are more than 3 times as likely as White individuals to develop ESKD, she said. Awareness of racial disparities in kidney risk is also imperative, St. Peter noted. African American individuals are more than 3 times as likely as White individuals to develop ESKD. Asian, Hispanic, and American Indian individuals are also at increased risk.

Counseling Points

Patients taking SGLT2 inhibitors need to be counseled about the adverse effects associated with these agents, including hypovolemia (when taken with diuretics), urinary tract infections, and genital yeast infections. Hines urges patients taking diuretics with SGLT2 inhibitors to increase their fluid intake and monitor their urine color to make sure they are not becoming dehydrated. In some cases, she advises decreasing the dose of the diuretic. Even though the black box warning for amputations has been withdrawn from SGLT2 inhibitors, Morello still advises patients taking these agents to check their feet daily for changes.

Although hypoglycemia is not usually a risk with SGLT2 inhibitor therapy, it is possible in patients taking other antidiabetics, particularly insulin. Hines often works with providers to decrease insulin doses by 10% to 20% in patients starting SGLT2 therapy. Pharmacists must be mindful of which drugs are excreted by the kidneys so doses can be adjusted as necessary as kidney function declines, St. Peter noted. This includes metformin and antibiotics.

Patients should be reminded to monitor their blood glucose and blood pressure and be made aware of the dietary and lifestyle changes that play a part in diabetes control. “We don’t want to lose sight of [the] big things, [such as how] controlling diabetes plays such a positive role in delaying the progression of kidney disease,” Morello said.

For references, visit drugtopics.com.

### TABLE 1

**ALBUMINURIA CATEGORIES IN CKD**

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>ALBUMIN-TO-CREATININE RATIO</th>
<th>TERMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>&lt; 30 mg/g</td>
<td>Normal to mildly increased</td>
</tr>
<tr>
<td>A2</td>
<td>30-300 mg/g</td>
<td>Moderately increased*</td>
</tr>
<tr>
<td>A3</td>
<td>&gt; 300 mg/g</td>
<td>Severely increased**</td>
</tr>
</tbody>
</table>

Terms Key: ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.
* Relative to young adult level.
** Including nephrotic syndrome (albumin excretion ACR > 2220 mg/g).
Source: National Kidney Foundation

### TABLE 2

**GFR CATEGORIES IN CKD**

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>TERMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1**</td>
<td>≥ 90</td>
<td>Normal or high</td>
</tr>
<tr>
<td>G2**</td>
<td>60-89</td>
<td>Mildly decreased*</td>
</tr>
<tr>
<td>G3a</td>
<td>45-59</td>
<td>Mildly to moderately decreased</td>
</tr>
<tr>
<td>G3b</td>
<td>30-44</td>
<td>Moderately to severely decreased</td>
</tr>
<tr>
<td>G4</td>
<td>15-29</td>
<td>Severely decreased</td>
</tr>
<tr>
<td>G5</td>
<td>&lt; 15</td>
<td>Kidney failure</td>
</tr>
</tbody>
</table>

Terms Key: CKD, chronic kidney disease; GFR, glomerular filtration rate.
* Relative to young adult level.
** In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfills the criteria for CKD.
Source: National Kidney Foundation
Black Market Boom: Protecting Pharmacy Data from Cybercrime

Personal health information is among the most valuable black-market data for cybercriminals to collect and sell. By Fred Gebhart

6 Steps to Protect Your Pharmacy From Cyberattack

Cybercrime is big business—up 127% in 2021 over 2020—according to information technology (IT) consultants at Agio. The 6 simple steps listed below can help protect your pharmacy:

1. Require all employees to use company email—never personal email—for business and remote access.

2. Use a virtual private network for remote access.

3. Invest in a health care IT security vendor and up-to-date business-grade hardware (firewall) and software (active end point detection and response/extended detection and response antivirus) security. Expect to spend $25 to $35 per device per month.

4. Train all users to avoid phishing and other email scams. When in doubt, don’t click!

5. Require—and use—strong passwords with 8 or more characters that include upper- and lowercase letters, numbers, and symbols. Change passwords on a regular basis, and never share or write down passwords.

6. Maintain an offsite backup with a third-party provider in addition to your pharmacy system provider’s backup. Typically, pharmacy vendors back up only patient-related data. If ransomware or other disaster strikes, you need to restore all your data, not just patient records.

Best Value Pharmacies is under attack. Every week, the 13 Dallas-Fort Worth, Texas, area stores stop multiple online attacks every week. Some cyberattacks are as obvious as the receipt of invoices from vendors the company has never used, sent from online accounts outside the United States, sometimes not even in English. Some of these attacks look like legitimate emails but carry hidden malware designed to open the company up to ransom and theft.

“Some of those cyberattacks have gotten through our outer defenses, firewalls, antivirus programs, and other protections,” said Jason Carter, chief technology officer at Best Value Pharmacies. “Luckily, we train all our employees to think before they click. Knock on wood—our staff have stopped the intruders.”

Best Value isn’t alone: Every pharmacy, large and small, as well as every health care provider and organization, is in the crosshairs. “Hackers see health care as low-hanging fruit,” Carter said. “Any organization that has protected health information [PHI] is a rich target. Independent pharmacies don’t always have the advanced firewalls and security that larger organizations have.”

“It’s all about value,” said R. Jeffrey Hedges, CDME, ABI, president and CEO of R.J. Hedges & Associates, a pharmacy compliance consultant group in New Florence, Pennsylvania. “The black-market value of a Social Security number is under $1, [and] a credit card [is] maybe $5,” he explained. Patient health records, on the other hand, are valued at $250. “It’s not a matter of if you will be attacked—it’s when and how you protect yourself.”

The Health Insurance Portability
and Accountability Act (HIPAA) of 1996 defines PHI as inclusive of any information within an individual’s health record that can identify them. Unlike a credit card that can be canceled, PHI can’t easily be canceled or changed. And because of that, misuse can generate illicit income for years after a breach has been identified and plugged.

**More Than PHI**

Pharmacies offer other targets for cyber criminals as well, including employee data and financial assets. Ransomware programs can be introduced into any computer system, often by opening an infected email attachment. These nefarious programs encrypt system data and hold it for ransom. Ransomware is widely available online and is often employed by groups with a global reach.

“These gangs carefully vet their targets before attacking,” said Nick Dorazio, president of LVTech LLC, a health care cybersecurity provider in Greensburg, Pennsylvania. “I’ve seen pharmacies hit for $10,000 ransom, and the same program used against larger pharmacies to collect millions. It’s a massive, organized operation run by people who go into the office every day, and their only job is to break into you.”

More than one-third of health care organizations in the United States were hit by ransomware attacks in 2020, Hedges said. Approximately 65% of these attacks were successful, and approximately one-third of the targeted organizations that had data stolen paid up. However, only 69% of organizations that paid ransom actually got their data back.

“Don’t think that just because you’re a small independent pharmacy that you’re safe,” said Dallas Moore, PharmD, MS, director of pharmacy informatics and technology at the University of Utah Health Hospitals and Clinics in Salt Lake City. “We are all targets, all the time. The problem is only going to get worse.”

ECRI, a global health care quality and safety group, identified cybersecurity attacks as the top health technology hazard for 2022—and insurance policies rarely cover the entire financial cost of a cyber breach, Hedges cautioned. Any HIPAA breaches can lead to massive fines that are not discharged in bankruptcy, and no insurance policy can restore patient trust lost in a cyber breach.

**A Safer Pharmacy**

“Protecting yourself starts with...educating [leaders and staff] about the risks and impact cyberattacks can have on your organization and patients,” said Melissa Skelton Duke, PharmD, MS, BCPS, FAPhA, executive director of population health pharmacy solutions at Banner Health in Phoenix, Arizona. “The second thing is to minimize the risk of cybersecurity attacks in day-to-day operations. It’s a cat-and-mouse game that is always evolving.”

Solid cybersecurity takes a layered approach. The first layer is a private domain, which enables company email, which is easier to secure than multiple employee email addresses. “We still see pharmacists using AOL for their email, which is anything but secure,” said Dalton Fabian, PharmD, data scientist at UnityPoint Health in Des Moines, Iowa. Cybersecurity starts with a firewall that can be tuned to stop threats from the outside, block outgoing connections to unsafe locations, and prevent downloads of content, such as online games that may harbor malware. A virtual private network encrypts traffic, a key safeguard when staffers log into the pharmacy system remotely. “Work with your IT vendor to design your protection, first by finding an IT security vendor who knows health care—preferably pharmacy,” Fabian said.

The next layer of security is antivirus. Dorazio recommended active EDR/XDR antivirus. With cybercrooks using artificial intelligence (AI) to create malware, pharmacies need AI protection. “EDR/XDR is AI-based to detect [emerging] threats,” he said, adding that these protections should be on each device.

The final layer is staff training. Phishing—emails designed to trick users into disclosing information, opening infected attachments, or visiting infected websites—is the source of most ransomware and other malware, Dorazio explained. Every person with any access to any part of the pharmacy system—from the owner to the newest part-timer—should be trained to recognize phishing.

“The most effective approach is a training session with a surprise phishing test from you or a security firm like ours,” he said. “[People] think that [instantly] tells you who got the message and who needs to pay more attention.”

The key is to look at where the email came from and where any active links lead, Dorazio explained. Before visiting any links, right-click to see the true source of an email and the true destination of a link. “Think before you click,” he said. “If there is one-half of 1% of doubt, don’t click on it. If you’re not expecting something, chances are it’s not real.”

For references, visit drugtopics.com.

**THINK before you CLICK.**

*If there is one-half of 1% of doubt, don’t click on it. If you’re not expecting something, chances are it’s not real.*

**Nicholas Dorazio, President of LVTech LLC**
Osteoarthritis (OA) is the most common form of arthritis, affecting more than 32.5 million adults in the United States. Although there is no cure for this degenerative joint disease, a variety of OTC medications can help with pain management, according to the American College of Rheumatology/Arthritis Foundation guidelines. Pharmacists can play a key role in counseling and recommending OTC pain management options.

**Dietary Supplements**

**Although glucosamine products are some of the most used dietary supplements in the United States, they should not be recommended for knee, hip, and/or hand OA. Many clinical trials have demonstrated a lack of benefit vs placebo.** Chondroitin sulfate, often found in combination with glucosamine, is also not recommended for knee and/or hip OA. However, it is conditionally recommended for hand OA. Patients taking anticoagulants (eg, warfarin) can have an increased risk of bleeding with glucosamine and chondroitin sulfate.

Because dietary supplements are not regulated by the FDA, patients should check their products for the USP Verified Mark to ensure the quality of the product.

**Oral Nonsteroidal Anti-inflammatory Drugs**

**KNEE**

- Glucosamine and chondroitin sulfate are not recommended.
- Ibuprofen and naproxen are most effective.
- Diclofenac gel is strongly recommended.
- Topical capsaicin is conditionally recommended.
- Acetaminophen is conditionally recommended.

**HIP**

- Glucosamine and chondroitin sulfate are not recommended.
- Ibuprofen and naproxen are most effective.
- Acetaminophen is conditionally recommended.

**HAND**

- Glucosamine and chondroitin sulfate are not recommended.
- Ibuprofen and naproxen are most effective.
- Diclofenac gel is conditionally recommended.
- Topical capsaicin is not recommended.
- Acetaminophen is conditionally recommended.

**Recommendations and Counseling Pearls**

**Before seeing a physician, patients can try to treat osteoarthritis pain with OTC remedies.**

By Jennifer Gershman, PharmD, CPh
drugs (NSAIDs), such as ibuprofen (Motrin) and naproxen (Aleve), are considered the most effective for knee, hip, and/or hand OA pain management. It is important to take these medications with food, and treatment should be for the shortest duration and at the lowest dose possible because of the risk of gastrointestinal (GI), cardiovascular (CV), and renal adverse effects. Patients may need GI prophylaxis with a proton pump inhibitor to reduce this risk.

Patients should be counseled on the signs and symptoms of CV problems—chest pain, shortness of breath or breathing difficulty, sudden weakness or numbness in one part or side of the body, or sudden slurred speech—and be directed to report those symptoms. The FDA previously strengthened the existing Drug Facts labels for all OTC nonaspirin NSAIDs to emphasize the increased risk of myocardial infarction (MI) and stroke. Patients with a history of MI or stroke should avoid oral NSAIDs.

Topical Agents
Topical NSAIDs have less risk of systemic exposure compared with oral agents. They are strongly recommended for knee OA and conditionally recommended for hand OA. Diclofenac 1% (Voltaren Arthritis Pain) should be applied on up to 2 joint areas 4 times daily to clean, dry skin. Patients should wash their hands thoroughly after applying the gel unless they are applying it to their hands. Remind patients to wash their hands 1 hour after application.

Diclofenac gel should not be applied to skin that is broken or infected, and patients should avoid the gel making contact with their eyes, nose, or mouth. Remind patients that the dosing card should always be used to measure a dose of this product. After 21 days, patients should consult a physician before further use. To minimize the risk of adverse effects, oral and topical NSAIDs should not be combined.

Topical capsaicin (Zostrix) is conditionally recommended for patients with knee OA but not for hand OA because of the risk of ocular adverse effects from potential contact. Topical capsaicin may need to be applied 3 to 4 times a day. It typically takes 2 to 4 weeks to see a benefit. Patients should wash their hands immediately after applying capsaicin. Capsaicin can cause a burning or stinging sensation. Remind patients not to apply the product to broken or irritated skin.

Acetaminophen (Tylenol)
Acetaminophen is conditionally recommended for patients with knee, hip, and/or hand OA. Evidence suggests it may not be the most effective medication for OA, but it can be an important treatment option for patients who are unable to take NSAIDs. The maximum daily recommended dose of 3000 mg to 4000 mg acetaminophen per day, depending on the product, should not be exceeded because of the risk of hepatotoxicity. Alcohol consumption should be avoided. To prevent potential overdose, it is critical to educate patients on the importance of reacing the product label to ensure that they are not taking multiple acetaminophen-containing products.

Although OTC products can help, patients should consult a physician if their OA is worsening or if their pain is not relieved by OTC treatments.

For references, visit drugtopics.com.

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Transparency is a buzzword these days. We hear about it on the nightly news in reports about our government, schools, restaurants, and even social media. Transparency in the pharmacy industry is undoubtedly an active discussion topic, and pharmacy owners have been fighting for it for years with little success. Let’s discuss some key areas where a lack of transparency hurts pharmacy owners and, ultimately, patients.

Controlled Medications
Because of past situations involving the overprescribing and overdispensing of controlled medication, both the Drug Enforcement Agency (DEA) and wholesalers closely monitor pharmacies’ ordering habits. On the surface, this is a good thing: No one is a proponent of pill mills. However, the lack of transparency in this process hurts pharmacy owners and patients.

Pharmacists will regularly turn away legitimate prescriptions from legitimate patients who present with a new controlled prescription. Why? Likely, these pharmacists are worried about going over ambiguous thresholds and ratio limits. The pharmacist is concerned that if they increase their purchases of these controlled substances, they will trigger a controlled medication audit and perhaps prevent the pharmacy from ordering what they need to fill prescriptions. This confusion comes from a lack of transparency from wholesalers and enforcement agencies.

The Worst-Case Scenario Does Happen
Many pharmacy owners have heard horror stories of pharmacies forced to close or their ability to order controlled medications taken away. For West Virginia pharmacist Martin Njoku, these horror stories became real life when the DEA raided Oak Hill Hometown Pharmacy and revoked Njoku’s right to dispense controlled substances. The raid, according to previous reporting, came a few years after Njoku began dispensing buprenorphine to customers, both local to Fayette County, West Virginia, and those displaced by flooding in nearby counties.

Although Martin was cleared of all wrongdoing, the damage was done. He was forced to close his pharmacy and his community lost critical access to the care it needed.

Drug Pricing
Another area that lacks transparency is drug pricing. From the patient’s point of view, there has been some significant, positive headway where drug pricing transparency is concerned. But, many pharmacies still deal with smoke-and-mirrors pricing in the drug acquisition process.

In the traditional wholesaler model, the pharmacy places orders for medication and pays an “invoice cost,” which is an inflated price for its inventory. The pharmacy can earn rebates over the next several months to lower its acquisition cost, but because rebates come in long after the medication is dispensed, pharmacies don’t know the actual cost of a product at the point of sale. They are left to make educated guesses.
percentage cap across an insurance’s pharmacy has a maximum profit.

Under an effective rate contract, the remuneration (DIR) fees.

2 most egregious culprits are effective rate contracts and direct and indirect business comes in many forms, but the side comes in many forms, but it also impacts both clinical decisions and the service offerings provided to their community. The purchasing process needs to be infused with transparency so pharmacy owners can focus on patient care instead of playing purchasing games.

Reimbursement Rates
A lack of transparency around pharmacy payments has the same deleterious effects as pharmacies not knowing drug costs. Frequently, pharmacists are left guessing how much money they are losing, or assuming they are making money only to never see those revenues realized.

Confusion on the reimbursement side comes in many forms, but the 2 most egregious culprits are effective rate contracts and direct and indirect remuneration (DIR) fees.

Effective Rate Contracts
Under an effective rate contract, the pharmacy has a maximum profit percentage cap across an insurance’s entire book of business. This cap causes a reimbursement amount at adjudication to become, essentially, a made-up number, with the payment processor guessing at what the rate should be. A “true-up” will happen later, typically resulting in the pharmacy paying back large sums of money to the pharmacy benefit managers. Pharmacy owners are left in limbo for months, wondering what their actual revenues will be. Any business owner can easily empathize with the trouble this unknowing causes.

DIR Fees
DIR fees for Medicare claims are the most significant source of concern for pharmacy owners. The lack of transparency comes from several questions:

- How much will the pharmacy be charged?
- How is the pharmacy graded?
- How can the pharmacy improve its performance?
- When will the pharmacy be charged?

While these seem like easy questions to answer, the lack of transparency makes answering nearly impossible. Each Medicare plan has published DIR fee ranges, but these ranges are wide and the difference to a pharmacy’s bottom line is critical if it is, for example, 11% vs 15%. There also never seems to be a straightforward answer for how each pharmacy earns its score and ensures the data are clean. A patient who passes away, for example, counts as missed fills, lowering the pharmacy’s adherence score for many months until the patient drops from its calculation. No one intended for deceased patients to cost pharmacies thousands of dollars.

Fighting For Transparency
Many pharmacy industry organizations and individuals are fighting long, hard battles to improve transparency throughout the industry. It is critically important to talk to your elected representatives at all levels of government and to support organizations like Pharmacists United for Truth and Transparency or the National Community Pharmacists Association in their quest for change. Most importantly, pharmacy owners must understand the impact that a lack of transparency has on their business. Knowing where there are information blind spots may help owners see the bigger picture and make better choices for patients and the pharmacy alike.

Are there any other areas where transparency would improve pharmacy practice? Email your comments to lbiscaldi@mjhlifesciences.com.

REFERENCE

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When Perfect Is the Enemy of Good

While volunteering at a COVID-19 vaccine clinic, our columnist learned about the benefit of lightening up.

Over the course of our 8-, 10-, or 12-hour days, we are required to be perfect.

We pharmacists are indeed a meticulous bunch, striving for perfection because we must be perfect. I gave a presentation once where I shared that, for pharmacists, 99.9% is not good enough. In my 40-year career, I have worked 7680 days. If on average I filled 200 prescriptions per day, that would be a total of 1,536,000 prescriptions in my 4 decades. If I had an accuracy rate of 99.9%, that would be 1536 errors—a number to keep any pharmacist awake at night!

We community pharmacists are loners, usually the only one on the bench for a period of time. So it was with great delight when I got tapped to help my wife, Denise, with her massive COVID-19 vaccination effort in State College, Pennsylvania. I stood back in amazement watching my “lab partner” take, with minute-to-minute precision, the vaccine from the dry ice, then to the refrigerator with digital data logger, then to the clinic site with prescribed hard-side cooler and digital data logger, where 2400 patients would be immunized. With stopwatch accuracy, she would chart when the vaccine was pulled from the refrigerator, then taken to the drawing room, where syringes were filled to exactly 0.3 mL after dilution with exactly 1.8 mL of saline. The syringes were put into a labeled bag and checked for accuracy and bubbles. The time was then written on the bag, to the exact minute.

At one point, the 2 pharmacists in the room were discussing the use of a 3-mL syringe to draw up 0.5-mL doses of the other vaccine. We learned during our first lab in pharmacy school that the minimum measurable quantity of any vessel was 20%: a 100-mL graduate should never be used to measure less than 20 mL; a 25-mL graduate never less than 5 mL, and, therefore a 3-mL syringe should never measure less than 0.6 mL. But the government had sent these 3-mL syringes to do just that: measure 0.5 mL. Beside me in the drawing room were several dentists, physicians, and nurses. One of these brilliant young physicians was Dr Mark Stephens, who works for Penn State Medicine. Stephens has a military background. He’s tall, muscular, and very personable. Hearing our discussion, Stephens replied in a way I won’t soon forget: “For crying in the bucket, we’re in the middle of a pandemic.”

At the last clinic, we were busy pulling up 0.25 mL booster doses. Lo and behold, we were given U-100 insulin syringes marked in units. Come on, ref…throw the yellow flag! Insulin syringes are never to be used to measure anything but insulin, and TB syringes are never to be used to measure insulin; this is a mortal sin in pharmacy practice. But Stephens just looked at us, smiled again and said, “For crying in the bucket, we’re in the middle of a pandemic.”

I’m not here to tell my fellow pharmacists to aim lower. In fact, in some cases aiming lower could produce tragic results. Over the course of our 8-, 10-, or 12-hour days, we are required to be perfect. Dispensing 119 tablets of hydrocodone in a prescription order that calls for 120 tablets is never good enough!

But sometimes in our day-to-day work, we need to lighten up on the rigorous rules we were indoctrinated with. Stephens has also been known to quote Voltaire, reminding us that “perfect is the enemy of good.” But my favorite quote of his goes back to his military days: “Sometimes, health care is like throwing hand grenades. Getting close is good enough to get the job done.” Lighten up, fellow pharmacists—we are doing one heck of a great job!

Peter A. Kreckel, RPh, practices community pharmacy in Lemont Furnace, Pennsylvania.
NEW DRUG REVIEW

Molnupiravir: Oral Antiviral for the Treatment of COVID-19

Gregory M. Mazzie, BS, and Cassandra R. Doyno, PharmD, BCPS, BCCCP

In December 23, 2021, the FDA issued an EUA for molnupiravir (Lagevrio). Molnupiravir is an oral antiviral developed by Merck for the treatment of confirmed mild to moderate COVID-19 in adults 18 years or older who are at high risk of severe disease. Molnupiravir is currently available by prescription only and should be initiated as soon as possible after COVID-19 diagnosis and within 5 days of symptom onset.

**Efficacy**

Results from a phase 3 randomized, placebo-controlled, double-blind trial support the EUA for molnupiravir. The MOVE-OUT trial (NCT04575597) evaluated 1433 nonhospitalized adults with mild to moderate COVID-19 and 1 or more predefined risk factors for disease progression. Participants were symptomatic within 5 days of randomization with a laboratory confirmed SARS-CoV-2 infection, and were excluded if previously vaccinated against SARS-CoV-2.

Primary efficacy end point was the percentage of patients who were hospitalized or died through day 29 due to any cause. In an interim analysis of 762 participants, 7.3% who received molnupiravir were either hospitalized or died through day 29 vs 14.1% of the placebo group, a 51% reduction. Adjusted risk difference was –6.8% (95% CI, –11.3% to –2.4%). Analyses were adjusted by the stratification factor of time of COVID-19 symptom onset (< 3 days vs > 3 [4-5] days).

**Safety**

The most common adverse events (AEs) included grade 1 or grade 2 diarrhea, nausea, and dizziness. Serious AEs occurred in 7% of participants receiving molnupiravir and were mostly COVID-19 related. The prescribing provider or provider designee is responsible for mandatory reporting of all serious AEs and medication errors potentially related to molnupiravir within 7 calendar days of event awareness. Molnupiravir may cause fetal harm and therefore is not recommended for use in pregnancy.

**Dosing and Special Considerations**

Molnupiravir is supplied as 200-mg capsules. Current dosing recommendation is 800 mg (four 200-mg capsules) taken orally every 12 hours for 5 days with or without food. Molnupiravir should be taken as soon as possible after COVID-19 diagnosis and within 5 days of symptom onset, as safety and efficacy for extended use past 5 consecutive days has not been established.

Completion of the full 5-day treatment course and continued isolation in accordance with CDC recommendations are important to maximize viral clearance and minimize transmission of COVID-19. If patients miss a dose within 10 hours of the scheduled time, the dose should be taken as soon as possible. If the missed dose is greater than 10 hours, the next dose should be taken at the scheduled time; do not double the dose. Dosing recommendations, safety, and efficacy have not yet been established in pediatric patients. There are currently no dosage adjustment recommendations based on renal or hepatic impairment or in geriatric patients. No significant drug interactions have been identified based on limited available data within the EUA.
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