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ISMP
An ECRI Affiliate

Community/Ambulatory Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

ISMP urges increased action at the practice level to halt the growing danger of counterfeit drugs

Problem: Counterfeit drugs, or fake drugs, made to resemble genuine pharmaceutical manufacturers' medications (**Figure 1**), have been a longstanding threat to the health and safety of patients. Alarmingly, this problem has grown far more ubiquitous in recent years. Most have attributed this rise to the skyrocketing profits made by criminal groups, the growth of unregulated online marketplaces posing as legitimate pharmacies, and the increasing use of social media to advertise counterfeit medications. For example, during the coronavirus disease 2019 (COVID-19) pandemic, more patients became accustomed to purchasing medications online. However, not all online pharmacies are created equal. According to the National Association of Boards of Pharmacy (NABP), about 95% of so-called online pharmacies operate illegally.[1] Lack of awareness and education about this issue results in serious risks to patients' lives.

In 2023, the Drug Enforcement Administration (DEA) seized more than 79.5 million fenta**NYL**-laced counterfeit tablets.[2] DEA testing shows as many as 7 out of 10 counterfeit medications contained a potentially lethal dose of fenta**NYL**. While anyone can unknowingly purchase counterfeit medications, young adults and individuals in marginalized groups are most at risk. According to the Centers for Disease Control and Prevention (CDC), fenta**NYL**-related adolescent overdose deaths tripled from 2019 to 2021. About a quarter of these deaths are linked to counterfeit medications.[3]

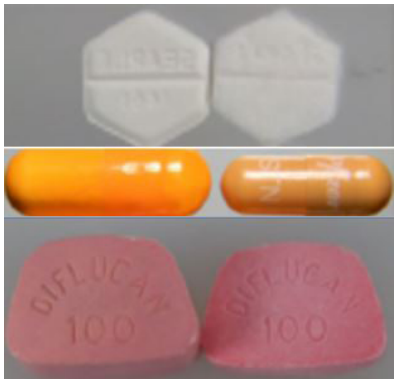

Figure 1. Examples of the medications (right side of each pair): **CYTOTEC** (mi**SOPROS**tol) (top), **SUTENT** (**SUNI**tinib) (middle), and **DIFLUCAN** (fluconazole) (bottom), along with counterfeit versions (left side of each pair).

More Than an Illicit Drug Problem

Counterfeit medications are often associated with illicit drug use, which may cause some people to believe "it can't happen to me." However, counterfeit drugs represent a serious threat to all, from young people seeking help with attention-deficit/hyperactivity disorder (ADHD) to elderly patients looking for the lowest price for their prescriptions. Examples of counterfeit drugs include chronic medications for diabetes and heart disease, cancer drugs, and antivirals for infectious diseases such as human immunodeficiency virus (HIV). Counterfeit drugs are frequently adulterated with potentially lethal ingredients including lead, mercury, toxins, or harmful chemicals. More troubling, as mentioned above, an increasing number of fake drugs are laced with fenta**NYL**, fueling the epidemic of overdose deaths plaguing the United States. Fenta**NYL** is now the leading cause of death for Americans aged 18 to 45.[4]

Even when not contaminated with dangerous material, counterfeit drugs often lack the required active ingredients to be effective. Their use can lead to treatment failures, complications, and other morbidities. They also impose significant economic burdens on patients and healthcare organizations due to the costs associated with ineffective treatments and management of prolonged illnesses

A Global Crisis

The World Health Organization (WHO) identified counterfeit medications as "one of the urgent health challenges for the next decade."[5] Fake drugs have become a big business globally–estimated

continued on page 2 — Counterfeit drugs >

SAFETY briefs

Kentucky law prevents practitioners from being criminally charged for medical errors. We were pleased to learn that Kentucky Governor Andy Beshear recently signed a bill (House Bill 159: www.ismp.org/ext/1363) into law that protects healthcare practitioners from being criminally charged for medical errors, making Kentucky the first state to do so. Under this bill, practitioners, including nurses, pharmacists, and physicians, "shall be immune from criminal liability for any harm or damages alleged to arise from an act or omission relating to the provision of health services" with exceptions for gross negligence and intentional misconduct.

ISMP, along with others, feared the criminal charges and the guilty verdict against RaDonda Vaught, who had been convicted of criminally negligent homicide and gross neglect of an impaired adult following the 2017 tragic death of Charlene Murphey, set a dangerous precedent with worrisome implications for safety (www.ismp.org/node/30908). We were concerned the guilty

continued on page 2 — SAFETY briefs >

IMPORTANT! Read and utilize the Community/Ambulatory Care Action Agenda

Items from the **January – April 2024** issues of the ***ISMP Medication Safety Alert! Community/Ambulatory Care*** newsletters have been selected and prepared for you and your staff to stimulate discussion and collaborative action to reduce the risk of medication errors. Each item includes a brief description of the medication safety problem, a few recommendations to reduce the risk of errors, and the issue date to locate additional information. The **Action Agenda** is available for download as an Excel file (www.ismp.org/node/133880).

> Counterfeit drugs — continued from page 1

to be worth as much as $431 billion a year.[6] According to WHO, counterfeit drugs account for roughly 10% of the medical products circulating in low- and middle-income countries, with an estimated one million people dying annually from taking fake or substandard medications.[7]

Counterfeit medications have entered the supply chain worldwide, including the European Union, Canada, and the United States. As the internet has become a global marketplace, it can be difficult for federal and state authorities to track and prosecute rogue sites, which sophisticated criminal networks often operate. Many illegal online pharmacies pass themselves off as Canadian pharmacies providing prescription medications at lower prices. Criminal groups may include the word "Canada" in their URL or show individuals dressed as medical professionals and a maple leaf symbol on their landing page, making it difficult to discern between a legitimate and fake site. Some online pharmacies source their drugs from other countries known to produce counterfeit medications.

Adverse Events

Whether they were aware of the scheme or not, some healthcare practitioners have been caught in the dark world of counterfeiters. For example, in 2021, two California oncologists pled guilty to purchasing more than $1 million of unapproved and counterfeit cancer drugs from a company owned by a Winnipeg internet pharmacy. The US Food and Drug Administration (FDA) found the discounted oncology drugs contained no active ingredients. Canadian authorities prosecuted and sentenced the owner of the Winnipeg internet pharmacy.[8]

We also shared concerns about the impact of counterfeit medication in our February 2024 newsletter article, *Increased demand and shortages of GLP-1 receptor agonists contributes to patient harm*. A hospital reported that, in less than a week, three patients required admission to the intensive care unit due to severe hypoglycemia from compounded semaglutide. The patients had received multiple pens without a prescription from people identified as "nurses" in a hotel room or a gathering akin to a "Botox party," and the drugs were thought to be counterfeit.

Safe Practice Recommendations: Pharmacies and other healthcare organizations have a crucial role in raising awareness of this threat to patients and should consider the following strategies:

Educate practitioners. Educate staff about the potential for patients to present to different healthcare settings (e.g., emergency department, physician's office, pharmacy) with adverse reactions after knowingly or unknowingly taking counterfeit medications. Monitor patients for unexpected outcomes (e.g., increased side effects, medication not working as it previously had) and consider if counterfeit medications could be the culprit. When reviewing a patient's medication history, include a scripted open-ended question asking where they obtain their medications.

Follow literature and media reports. Maintain an awareness of publicized incidents and the medications involved to focus on known problem drugs and pharmacological categories.

Educate patients. Pharmacists, prescribers, and nurses are among the most trusted sources of medical information and uniquely positioned to educate patients about the risk of counterfeit drugs. Proactively have professional staff share with patients the warning signs that may indicate a pharmacy could be selling counterfeit drugs. Refer patients to the ISMP consumer website (www.ismp.org/ext/1383) and FDA's BeSafeRx campaign (www.ismp.org/ext/618). Even when comparing counterfeit and real medications side-by-side, it can be difficult to tell the difference without laboratory testing. However, there are important safety tips that patients can consider when purchasing medications:

Use a verified pharmacy. When patients are considering using an online pharmacy for their prescriptions, educate them about the National Association of Boards of Pharmacy's (NABP's) searchable list of accredited online pharmacies (www.ismp.org/ext/1344) that comply with quality

continued on page 3 — Counterfeit drugs >

>SAFETY briefs

cont'd from page 1

verdicts would discourage practitioners from reporting errors, undermine the creation of a culture of safety, accelerate the exodus of practitioners from practice, perpetuate the myth that perfect performance is achievable, and impede system improvements. We are thankful for the path Kentucky has taken with this new law. We hope similar actions will be taken by other states.

Wrong drug error following the use of an abbreviation. A prescriber intended to start a patient on human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) and ordered **CABENUVA** (cabotegravir/rilpivirine) injection along with an oral lead-in regimen of **VOCABRIA** (cabotegravir) and **EDURANT** (rilpivirine). While this is an appropriate regimen for treatment of an HIV infection, it is not for PrEP. Instead, an appropriate PrEP regimen is **APRETUDE** (cabotegravir) injection and an oral lead-in with Vocabria. An oral lead-in is a short-term use of oral therapy used to assess medication tolerability before transitioning to a long-acting injectable form of therapy. The use of the wrong regimen exposes the patient to inappropriate antiretroviral medications which may lead to the development of HIV drug resistance and future harm.

The prescriber in this scenario routinely used the unsafe abbreviation "CAB" for cabotegravir. When prescribing the medication, they inadvertently selected, Cabenuva, in the electronic health record (EHR), which starts with "CAB," instead of Apretude (cabotegravir). This prescription was sent to the health system's specialty pharmacy. The prescriptions for the oral lead-in therapy (Vocabria and Edurant) were sent to an outside specialty pharmacy authorized to dispense the limited distribution drug Vocabria (the health system pharmacy did not have access to Vocabria). When a pharmacist at the health system pharmacy was verifying the Cabenuva prescription, they reviewed the patient's medical record and noted that the patient was HIV-negative and therefore not a candidate for Cabenuva. The prescriber was notified, and they alerted the patient to stop taking Edurant

continued on page 3 — >SAFETY briefs >

> Counterfeit drugs — continued from page 2

assurance criteria. You can also report suspicious online pharmacies via this website. With any online pharmacy, patients should see if there is a licensed pharmacist available who can answer questions about the medication. This is not only helpful when seeking information, but also speaks to the legitimacy of the pharmacy.

Check for spelling errors. Review packages and labeling for spelling errors. Misspellings anywhere on the packaging (e.g., product name, manufacturer, main ingredients on bottle label) are one of the most noticeable mistakes on counterfeit products.

Evaluate medication appearance. Inform patients that, although manufacturers might change products or pharmacies might provide different generic products, any concerns about differences in size, color, or shape of the medication when the prescription is filled should be addressed. For this reason, it is best to obtain a refill shortly before the current prescription is finished. Educate patients to compare the new medication and packaging with the previously filled medication. Patients should note any differences and ensure the drug description on the new pharmacy label matches that of the drug inside the container. If they have any questions, patients should consult their prescriber or pharmacy before taking the medication.

Assess medication quality. Legitimate medications will have a factory-made appearance. If tablets are cracked, have a bubbled-up coating, are crumbly or moldy, or come in jars containing excess powders or crystals, patients should be suspicious. Medications that come in the original manufacturers' packaging should be sealed. If the package has been opened, has a broken seal, appears to have been tampered with, comes in different or no packaging, is missing the label, or just does not look right, patients should check with a healthcare practitioner before taking the medication.[9]

Report concerns. Law enforcement cannot stop the dangerous flow of counterfeit drugs without the support of public and private stakeholders. Many private sector companies have counterfeit drug operations dedicated to supporting law enforcement efforts. Some manufacturers have a team that investigates possible criminal groups creating and distributing counterfeits and have forensic laboratories with scientists who specialize in analyzing and tracking counterfeit medicines. Practitioners should also be aware of and share resources from government agencies that offer information to combat counterfeit drugs, such as:

- CDC (www.ismp.org/ext/1346)
- FDA (www.ismp.org/ext/1347)
- The National Intellectual Property Rights Coordination Center (www.ismp.org/ext/1348)

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continued in the column to the right >

>SAFETY briefs cont'd from page 2

but continue Vocabria. The prescription for Cabenuva was discontinued and Apretude was dispensed instead.

To prevent similar medication errors, avoid using drug name abbreviations, such as "CAB," when referring to medications. Check your EHR and order entry systems to ensure antiretroviral abbreviations are not automatically populated or included in the drug name fields. Use brand and generic names when referencing HIV products. Create or update order sets for HIV treatment and PrEP. Prescribers should provide the appropriate indication for a medication on the prescription. Ideally, electronic prescribing systems would foster this process by automating the inclusion of this information. Pharmacies should always verify an appropriate indication when dispensing medications, and they should check the patient's HIV infection status prior to dispensing HIV treatment, PrEP, or post-exposure prophylaxis (PEP) medications. Educate pharmacy and clinic staff about the risk of mix-ups with these drugs and regimens to raise awareness.

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Report medication and vaccine errors to ISMP: Please call 1-800-FAIL-SAF(E), or visit www.ismp.org/report-medication-error. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

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