August 2024 | Volume 22 ■ Issue 8

ISMP
An ECRI Affiliate

Nurse AdviseERR®
Educating the Healthcare Community About Safe Medication Practices

Drug diversion prevention beyond controlled substance medications

Controlled substance medications are most often thought of as being associated with substance use disorder and are most commonly the subject of diversion detection programs. However, non-controlled substances can be targeted by practitioners as well. Some medications may be targets of diversion due to their high street value and/or ease and ability to be sold illegally. Another possibility is that they may be diverted for self-use, for family/friends to self-medicate, or for those who cannot afford the cost of certain life-saving medications.

Non-controlled medication targets of diversion include high-value medications such as antiretroviral agents, certain cancer medications, performance-enhancing agents like erythropoietin, and psychoactive medications (e.g., cyclobenzaprine, **QUE**tiapine, tra**ZOD**one). Additionally, medications associated with opioid use disorder such as diphenhydr**AMINE** (to reduce opioid histamine-induced pruritis), ondansetron (to control nausea and vomiting related to opioid withdrawal), and naloxone (in case of an overdose) may also be diverted.[1-4]

The drug diversion program manager, Mary Nelson, from HonorHealth in Phoenix/Scottsdale, AZ, presented information on this topic during a November 2023 Medication Safety Officers Society (MSOS) member briefing. She noted that organizations often do not include non-controlled substances as part of their diversion detection programs because they may not understand the rationale as to why practitioners may be diverting non-controlled substances, or they might not know how to monitor them. In turn, practitioners may perceive non-controlled medications as easier to divert because they know that most organizations do not have processes in place to monitor them as closely.

Practitioners who divert non-controlled substances may be self-treating medical conditions (e.g., depression, anxiety) or selecting medications that have a synergistic effect to enhance the effect of other drugs (e.g., sedation, euphoria, dissociation). Practitioners may also dilute or swap patients' controlled drugs for non-controlled drugs (e.g., oxy**CODONE** for acetaminophen) keeping the controlled drugs for self-use or distribution, or they may use the non-controlled drug as a substitute for controlled waste resolution. As a result of this diversion, patients may experience lapses in care (e.g., untreated pain, therapeutic failure), or suffer harm (e.g., side effects, adverse reactions) from unknowingly receiving medication they were not prescribed. There is also the serious risk of patient harm due to substandard care from a practitioner impaired by the non-controlled substance. Finally, practitioners whose diversion compromise vials and syringes, place patients at risk for bloodstream infections.

Potential non-controlled substance diversion scenarios

*When reviewing a report that captured medications removed via override in an automated dispensing cabinet (ADC), a pharmacist noticed a trend with injectable diphenhydr**AMINE**. When a pharmacist investigated further, it was discovered that a specific nurse had several "override canceled" transactions for diphenhydr**AMINE** that occurred before the start of each shift. The pharmacist and nurse manager reviewed the nurse's transactions via surveillance videos, which showed that the nurse removed a vial with each canceled transaction. The diversion response team was consulted, and the investigation confirmed the nurse was diverting diphenhydr**AMINE**.*

A pharmacy technician could not locate a bottle of oral ondansetron that had been set aside to be

continued on page 2 — **Drug diversion** >

Sidebar

Is your organization's medication surveillance system positioned to detect foul play? We were devastated to learn about the case where a Pennsylvania nurse killed patients in nursing homes with lethal doses of insulin (www.ismp.org/ext/1366). After allegedly administering high doses of insulin to 22 patients at different facilities between 2020 and 2023, she recently pleaded guilty and was sentenced to three consecutive life sentences for first-degree murder charges and up to 760 years for criminal intent to commit murder. This caused us to pause and ask, how did something like this happen and continue for 3 years at different facilities? The following discussion explores that question and provides recommendations to help organizations address similar concerns.

The main article in this newsletter discusses how controlled substance medications are the most common targets for diversion detection programs, but that medication diversion by practitioners can involve non-controlled substances as well. Organizations often do not include non-controlled substances as part of their diversion detection programs because they may not understand the rationale as to why practitioners may be diverting non-controlled substances, or they may not know how to monitor them. In turn, practitioners may perceive non-controlled medications as easier to divert because they know that most organizations do not have processes in place to monitor them as closely. In this case, insulin was being diverted and administered to patients regardless of whether they had diabetes.

Please refer to the recommendations listed in the main article to address drug diversion of non-controlled medications within your organization. In addition, monitor patients for unexpected outcomes (e.g., increased side effects) and consider if foul play is involved.

> **Drug diversion** — continued from page 1

placed in unit dose packages. After searching the pharmacy and inquiring with staff, the technician contacted the pharmacy purchaser to order a replacement bottle. The purchaser recalled that this was not the first time ondansetron had been missing and notified the pharmacy manager. Video surveillance revealed that a pharmacist had been diverting the medication for self-use.

See the **Sidebar** article, on page 1 in the right hand column, about a recent non-controlled drug diversion case in Pennsylvania with fatal outcomes.

Recommendations

To prevent non-controlled medication diversion, senior leadership, including nursing leadership, within organizations should start by reviewing **Part I** of our previous publication, *Controlled substance drug diversion by healthcare workers as a threat to patient safety* (www.ismp.org/node/75668), which highlights the widespread scope of diversion in healthcare, barriers to recognition, at-risk behaviors, and other signs associated with possible diversion; and **Part II** (www.ismp.org/node/80596), which includes tools for preventing, identifying, reporting, and responding to diversion. ISMP has also provided webinars on diversion which can be found in our on-demand education library (www.ismp.org/ext/1404). Use this information as a starting point for drug diversion response programs and then incorporate medications beyond controlled substances by considering the following recommendations:

List non-controlled drugs at risk for diversion. Based on your organization's formulary, an interdisciplinary diversion response team (which includes representatives from nursing), ideally led by a dedicated diversion officer, should develop a list of non-controlled substances that organizations should monitor or treat similarly to controlled substances (see the examples in the second paragraph of this article). Use this list to address storage configurations of non-controlled substances at risk of diversion. Consider treating these drugs like controlled substances, including requiring a blind count (meaning that staff are not aware of the quantity in the inventory system prior to performing counts).

Monitor pharmacy inventory. Pharmacy leadership should use data from pharmacy inventory management systems and monitor the potential for non-controlled substance diversion within the pharmacy. Consider excessive restocking or running out of supply faster than expected when monitoring procurement, current inventory, and usage as potential signs of diversion.

Consider diversion analytics technology. Machine learning diversion monitoring and advanced analytics software programs use consolidated data sets from multiple informatics technology systems (e.g., ADCs, electronic health records [EHRs], attendance software, inventory systems, wholesalers) to reconcile stock movement and waste documentation, compare clinical data (e.g., pain scores) with dispensing patterns, detect when staff are accessing ADCs in areas where they do not normally work or are not scheduled to work that day, and trend behavior against other users on the same unit. If using diversion analytics technology, the interdisciplinary team should review this data that includes transactions of both controlled and non-controlled substances.

Evaluate the override list. Through the Pharmacy and Therapeutics (P&T) Committee or equivalent interdisciplinary group, review and approve all medications allowed via ADC override and the indication for removing the medication, clinical locations where staff can remove the medications via override, practitioner types who can remove medications via override, and associated policies. During the evaluation process, special attention should be paid to medications that are on the organization's non-controlled substance diversion list. Review the list of medications available by override at least annually and adjust as needed.

Monitor ADC data. Evaluate dedicated targeted reports with a regular cadence (e.g., daily, weekly, monthly) and designate an individual responsible for the review. Based on the organizational non-controlled drug diversion list, analyze ADC data such as canceled transactions, overrides, inventory

continued on page 3 — **Drug diversion** >

Worth repeating...

Entire bottle of nitroglycerin given at once, again!

This may sound unbelievable, but we recently received another report in which an entire bottle (25 tablets) of sublingual nitroglycerin (**Figure 1**) was administered to a patient. ISMP has reported on this exact error type on previous occasions including newsletters in 2007, 2017, and most recently in 2018. During orientation, an inexperienced nurse asked their preceptor, "Do I give one?" The preceptor said, "Yes," but it was not clearly communicated as one tablet versus one bottle. In addition, the automated dispensing cabinet (ADC) drug description stated, "nitroglycerin SL 0.4 mg (25 each)." So, the new nurse scanned the bottle, which did not alert them to administer only 1 tablet and proceeded to administer all 25 tablets. We do not know if the patient was harmed.

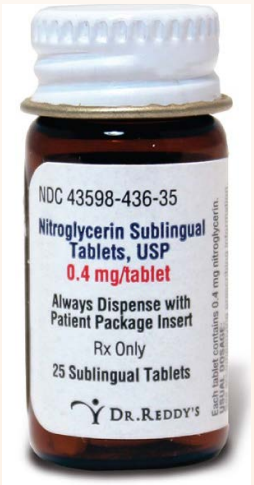

Figure 1. An entire bottle of 25 nitroglycerin tablets was given to a patient.

Most nurses are familiar with medications being provided in unit dose packages; typically holding a single dose for patient administration. Occasionally, a very small vial or bottle of medication is dispensed that contains more than one dose, and an assumption is made that it also must contain a single patient dose. We often caution practitioners, manufacturers, and compounders against placing multiple doses in one container, but in some cases that is not possible. Nitroglycerin tablets are one example.

Because of stability issues, nitroglycerin tablets must be dispensed in their original 25-count amber glass bottle and cannot be unit dosed. For charging purposes, order entry systems require a dispense quantity

continued on page 3 — *Worth* repeating >

> **Drug diversion** — continued from page 2

counts, and discrepancies for unusual or repetitive transactions. If a staff member is identified as an outlier when it comes to high usage of a non-controlled substance on the organizational list (e.g., diphenhydr**AMINE**), this may be the first sign of potential diversion and should be further investigated.

Establish reporting procedures. Provide a way for employees to proactively report suspected drug diversion via a confidential reporting portal or hotline. Make sure staff members who express concerns or suspicions about colleagues will be protected from retaliation.

Investigate and respond. If diversion is suspected, review the "all transaction" report from the ADC, EHR, surveillance videos, and badging access system. Discuss the findings of the initial investigation with an interdisciplinary diversion response team to determine the next steps. Depending on the team's recommendation, staff may need to be interviewed. Findings should be reported back to the team. While there may be a need to comply with reporting to relevant state and federal agencies, establish a culture of recovery, not solely punishment, for a healthcare worker who is diverting drugs. Include a process to determine the worker's employment disposition, and provide resources, such as access to employee assistance programs, for staff who may have a substance use disorder.

Educate staff. During orientation and at least annually, educate staff about the non-controlled substances that are commonly diverted. Outline the steps implemented to prevent drug diversion, the signs of drug diversion, and how to report and respond to drug diversion. Encourage staff to speak up when it comes to any medication they suspect is being diverted. To alleviate reporting concerns, educate staff on how to report using the reporting platform, and that confidentiality will be maintained to protect them from retaliation.

Evaluate. Organizations should immerse the drug diversion program in continuous process improvement. Gather feedback from staff, review internal and external data, and adjust processes as needed.

We thank Mary Nelson, MSN, RN, CCPS, for sharing a systematic review of HonorHealth's drug diversion program, as well as helping to write this article. Email ISMP (ismpinfo@ismp.org) with questions for HonorHealth.

References

1) National Institute on Drug Abuse (NIDA). Misuse of prescription drugs research report. What classes of prescription drugs are commonly misused? National Institute on Drug Abuse. June 2020. Updated June 12, 2023. Accessed December 19, 2023. www.ismp.org/ext/1061

2) Knight T. Is your organization protected from diversion of high-value drugs? *Healthcare Business Today*. December 9, 2021. Accessed December 19, 2023. www.ismp.org/ext/1068

3) Dinwiddie AT, Tanz LJ, Bitting J. Notes from the field: antihistamine positivity and involvement in drug overdose deaths - 44 jurisdictions, United States, 2019-2020. *MMWR Morb Mortal Wkly Rep.* 2022;71(41):1308-10. www.ismp.org/ext/1286

4) Kurtz SP, Buttram ME, Margolin ZR, Wogenstahl K. The diversion of nonscheduled psychoactive prescription medications in the United States, 2002 to 2017. *Pharmacoepidemiol Drug Saf.* 2019;28(5):700-6.

what's in a Name?

The "-tadine" drug stem name

Certain medications ending with the suffix "-tadine" belong to a class of medications known as histamine-1 (H1) antagonists, or simply called "antihistamines." It is important to note that not all medications with the "-tadine" suffix belong to this class of medications, and not all

continued on page 4 — what's in a Name? >

>Worth repeating

cont'd from page 2

of 25 tablets even though the dose is just one tablet at a time. So, scanning the label will not cause an alert that the quantity in the bottle does not match the amount to be administered. In fact, no alert was issued when scanning the bottle, so it was believed the amount in the container was the correct dose.

Since this is not the first time we have written about this issue, we are concerned that organizations do not believe it can happen in their facility and have not heeded our warning. Before another patient is harmed, we thought it was ***Worth* repeating**. To help avoid this type of error, ensure the medication administration record (MAR) and ADC screens denote 1 tablet = 0.4 mg, and include instructions to administer just 1 tablet sublingually (with additional doses as prescribed). The ADC drug description should specify it is a multi-dose vial (e.g., 25 tablets/multi-dose vial). Pharmacies should consider placing a flag label on the glass bottle with this same information and noting this is a multi-dose vial. Packaging the nitroglycerin bottle in a plastic bag or plastic amber prescription vial and affixing a label listing the per tablet strength and notation to administer just 1 tablet per dose, is also an option. Remind all practitioners when preparing or administering any medication, "If you need more than 3 (tablets, vials, or other dosage form), call the pharmacy."

More mix-ups between EPINEPHrine and ePHEDrine

A pharmacy technician stocked vials of e**PHED**rine in **EPINEPH**rine pockets in several ADCs. The products, **ADRENALIN** (**EPINEPH**rine) 1 mg/mL injection (Par Pharmaceutical), and e**PHED**rine 50 mg/mL injection (Amneal), come in similar-looking 1 mL vials with purple caps (**Figure 2**, page 4). Fortunately, the error was caught before reaching a patient, but we have previously reported similar mix-ups with these products.

These drugs also have known look-alike generic names and share indications that make storage of both products likely in the

continued on page 4 — *Worth* repeating >

what's in a Name?

continued from page 3

medications within this class end with this suffix. However, the focus of this article is on the "-tadine" antihistamines.

Antihistamines are commonly used to reduce allergy symptoms (e.g., itching, sneezing, runny nose [rhinitis], red itchy eyes [conjunctivitis]). Histamine, a chemical released during an immune response, is responsible for causing allergy symptoms. So, antihistamines work by blocking histamine at the H1 receptor site.

There are currently four single-agent antihistamines that contain this stem name (**Table 1**). In addition to being available as single agents, both loratadine and desloratadine are also available in combination with the decongestant pseudoephedrine. Pseudoephedrine works synergistically with the antihistamine to reduce congestion and sinus pressure. Olopatadine is also available in combination with mometasone, a corticosteroid, which helps treat the symptoms of seasonal allergic rhinitis. Cyproheptadine is available as an oral liquid and tablet and is more commonly used for other indications (e.g., appetite stimulation, cyclic vomiting).

Most of these antihistamines are available as oral formulations (e.g., tablets, capsules, liquids) to systemically treat allergic symptoms. However, olopatadine is available as both a nasal and ophthalmic formulation to directly target nasal and eye allergy symptoms. And, as stated earlier, the olopatadine combination product is only available as a nasal formulation.

Antihistamines are usually well tolerated and have few side effects. Common side effects from systemic antihistamines include somnolence/sedation, dizziness, drowsiness, fatigue, and headache. The nasal formulations can have more localized side effects such as nasal irritation and epistaxis (nasal bleed), in addition to causing a bitter taste, headache, and sinus pain. The ophthalmic formulations can also have more localized side effects such as abnormal sensation in the eyes, blurred vision, dry eye syndrome, burning sensation of the eyes, and eye pain. It is important to educate patients about these side effects and to report any concerns to their healthcare provider. Patients with impaired renal or hepatic function should use antihistamines with caution. Hypertension, cardiovascular disease, urinary retention, increased ocular pressure are relative contraindications to the use of antihistamines.

Table 1. Antihistamines with the suffix "-tadine" available in the United States.

Generic name(s)	Brand name(s)
cyproheptadine	generic only
desloratadine	**CLARINEX**
desloratadine and pseudoephedrine	**CLARINEX-D 12 HOUR**
loratadine	**ALAVERT**, **ALLERGY RELIEF**, **CHILDRENS LORATADINE**, **CLARITIN**, **CLARITIN ALLERGY CHILDRENS**, **CLARITIN CHILDRENS**, **CLARITIN REDITABS**, **FT ALL DAY ALLERGY RELIEF**, **FT ALLERGY CHILDRENS**, **GOODSENSE ALLERGY RELIEF**, **LORADAMED**, **LORATADINE CHILDRENS**, **TRIAMINIC ALLERCHEWS**
loratadine and pseudoephedrine	**ALAVERT D-12 HOUR ALLERGY AND CONGESTION**, **ALLERGY RELIEF-D**, **CLARITIN-D 12 HOUR ALLERGY & CONGESTION**, **CLARITIN-D 24 HOUR ALLERGY & CONGESTION**, **LORATADINE-D 12 HOUR**, **LORATADINE-D 24 HOUR**
olopatadine	Nasal formulation: generic only
	Ophthalmic formulations: **FT EYE ALLERGY ITCH & REDNESS**, **FT EYE ALLERGY ITCH RELIEF**, **PATADAY**
olopatadine and mometasone	**RYALTRIS**

>Worth repeating

cont'd from page 3

same clinical setting. As a vasoconstrictor, **EPINEPH**rine is 100 to 1,000 times more potent than e**PHED**rine, and mix-ups between these drugs have resulted in patient death (www.ismp.org/ext/1227).

Figure 2. Adrenalin (**EPINEPH**rine) and e**PHED**rine 1 mL vials with purple caps.

Require barcode scanning when dispensing, restocking, and administering these medications. Consider purchasing an alternative brand for e**PHED**rine with a different cap color. If possible, use prefilled commercially available or outsourcer-supplied **EPINEPH**rine syringes. Require the pharmacy to prepare infusions and bolus doses for these drugs except in emergencies.

ISMP Nurse *AdviseERR* (ISSN 1550-6304)

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.

Editors: Ann Shastay, MSN, RN, AOCN; Shannon Bertagnoli, PharmD; Rita K. Jew, PharmD, MBA, BCPPS, FASHP. ISMP, 5200 Butler Pike, Plymouth Meeting, PA 19462. Email: ismpinfo@ismp.org; Tel: 215-947-7797.