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Educating the Healthcare Community About Safe Medication Practices

Controlled substance drug diversion by healthcare workers as a threat to patient safety—Part I

Drug diversion by healthcare workers is a clandestine activity and is certainly underestimated and underreported.[1] Practitioners see firsthand the clinical effects of medications on patients, and many who divert drugs may harbor the false belief that they are in control of the situation and unlikely to harm patients or become addicted themselves.[2] Besides significant legal, financial, and personal risks that healthcare workers take when diverting medications, the true cost of drug diversion includes considerable risk downstream to unknowing bystanders, including healthcare facilities, the public, and especially patients. Pressures related to the coronavirus disease 2019 (COVID-19) pandemic have contributed to increased rates of anxiety in general, and this has certainly impacted healthcare workers. Coupling that with opportunities to easily access controlled substances, sets the stage for increased potential for diversion, making this a timely issue.

The most commonly diverted medications in healthcare include opioids, particularly **HYDRO**morphone, morphine, fenta**NYL** (including patches), **HYDRO**codone, oxy**CODONE**, methadone, and **SUBOXONE** (buprenorphine/naloxone); propofol; central nervous system depressants such as benzodiazepines (e.g., **ALPRAZ**olam, clonaze**PAM**); sedative hypnotics; and stimulants such as dextroamphetamine and methylphenidate.[3] While these medications are most likely to be associated with substance use disorder, and are the most common targets for diversion detection programs, it is important to note that diversion involves all prescription drugs. Other targets include high-value (high-cost) medications that could be sold or used for family members such as antiretroviral agents and certain cancer medications; performance-enhancing agents like erythropoietin and anabolic steroids; and other medications associated with opioid use disorder such as ondansetron (to control opioid withdrawal symptoms) and naloxone (in case of an overdose).[3-5] However, the focus of this article is controlled substance diversion as a risk to patient harm.

In **Part I**, we will discuss drug diversion, as it impacts patient safety. In **Part II**, which will be published in an upcoming issue, we will provide recommendations for implementing a proactive approach to prevent, identify, report, and respond to healthcare worker controlled substance diversion.

Definition

According to the National Association of Drug Diversion Investigators, drug diversion is a medical and legal concept involving the illegal movement, adulteration, marketing, or transfer of any legal controlled substance anywhere within the supply chain, from the manufacturer to the end user.[6] Diversion occurs whenever a medication is redirected from its intended destination, for personal use, sale, or redistribution to others.

Scope

One in 10 healthcare workers misuse drugs (or alcohol) during their career, which is similar to the percentage seen in the general population; however, the diversion trend is slightly different in healthcare, as workers in this setting are more likely to misuse prescription drugs rather than illicit drugs.[7] Drug diversion is thought to occur in all facilities that handle controlled substances.[1,8] A 2020 survey of healthcare executives showed that 96% agreed that drug diversion is occurring in US hospitals.[9] Many healthcare workers who divert drugs start with injectables.[4] In fact, tampering with an injectable medication, or removing the medication from a syringe or vial and replacing or diluting it with saline, water, or another substance, is the most serious type of drug diversion because it likely results in patient harm and is a desperate sign of a worker struggling with

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what's in a Name?

The "-tecan" drug stem name

Medications with the suffix "-tecan" belong to a class of chemotherapy agents referred to as topoisomerase I inhibitors. Topoisomerase I is an enzyme that plays an important role in cell replication. The "-tecans" bind to topoisomerase I which inhibits cell replication and thus, leads to apoptosis, or cell death. There are five "-tecans" approved for use in the United States; see **Table 1**.

Table 1. Medications with the suffix "-tecans" available in the United States.

Generic Name	Brand Name
irinotecan (conventional)	**CAMPTOSAR**
irinotecan (liposomal)	**ONIVYDE**
topotecan	**HYCAMTIN**
fam-trastuzumab deruxtecan	**ENHERTU**
sacituzumab govitecan	**TRODELVY**

Topoisomerase I inhibitors are used to treat a variety of cancers including, but not limited to, cervical, colorectal, central nervous system, breast, lung, and gastric cancers. Two of the "-tecans" are combined with antibody drug conjugates which are highly targeted biopharmaceutical drugs. The combined drug becomes more selective in targeting certain cells (cancer cells) and expresses fewer toxic effects on normal, healthy cells. For example, the antibody conjugate of Trodelvy binds to epithelial cancer cell surfaces and the antibody conjugate of Enhertu binds to human epidermal growth factor receptor 2 (HER2), thereby being more effective against certain aggressive metastatic breast cancers.

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addiction.[8] The COVID-19 pandemic has made the detection of diversion more difficult. In 2020, almost half (47%) of surveyed healthcare executives reported that staff turnover due to COVID-19 made it more difficult to track drug diversion, and more than one out of three (38%) had to cut their budget allocated to diversion investigations during the pandemic.[9]

Methods of Diversion

Medication-use processes in acute care settings are complex and involve many handoffs as medications move through the facility. Therefore, the methods used for drug diversion are often numerous, creative, and varied, and may occur during receipt, storage, compounding, dispensing, retrieval from storage locations, administration, and disposal to name a few.[4]

For example, in the main article, *Partially filled vials and syringes in sharps containers are a key source of drugs for diversion* (www.ismp.org/node/448), in our April 2016 newsletter, a 36-year-old nursing assistant who had been diverting discarded drugs died after self-administering what they likely thought might be an opioid but was actually a neuromuscular blocking agent.

In 2004, we heard about an incident involving Carpuject syringe tampering. Some controlled substances and other medications are provided in boxes of 10 tamper-resistant Carpujects, with syringes in two bundles of five, held together by a clear, wide plastic band. Unless they are properly inventoried, they can also facilitate drug diversion, and possibly even contribute to medication errors. A pharmacist reported that they noticed three instances in which someone had slipped an opioid syringe out of a bundle and swapped it with a promethazine syringe. In another case, someone replaced morphine 8 mg Carpuject syringes with 2 mg and 4 mg syringes. If a nurse is focused on confirming that the bundle of syringes is sealed and intact, a swapped syringe might not be identified during controlled substance counts, unless each label is checked. It is also possible to turn the Carpuject so the drug name is towards the middle of the bundle, making identification more difficult. Pharmacists have also missed swapped syringes when products were returned to the pharmacy. Unless you take the time to inspect the drug name on each syringe, you could easily assume that the count is correct if the number of syringes matches the expected quantity.

Aside from the obvious drug diversion problem, storing a medication in the wrong box may lead to an error. A nurse, for example, may unknowingly remove a syringe from the **HYDRO**morphone box without closely reading the label, assume that it is indeed **HYDRO**morphone, and then mistakenly give the wrong drug to the patient. Keep in mind, that the syringe packaging is tamper resistant, not tamper proof. People have always found ways to defeat safeguards (e.g., prying off seals, slitting plastic containers, regluing dust caps). An informed clinician who understands this risk, and why the syringe labels need to be read during controlled substances counts, can make it more likely to catch any diversion activities and prevent patient harm.

Outcomes

As previously stated, drug diversion is not a victimless crime; it not only causes harm to healthcare workers who divert drugs, but also to their coworkers, employers, and patients. Healthcare workers who divert medications risk criminal prosecution, medical malpractice lawsuits, loss of professional license/career, substance use disorder, overdose, and death. Coworkers may be forced to pick up an impaired colleague's workload or may feel guilty for not identifying the signs or speaking up. Employers bear the burden of fines, loss of Medicare and Medicaid reimbursement eligibility, civil and regulatory liability, and compromised public trust.[1] But the risks of drug diversion for unsuspecting patients are especially daunting. These risks include outright theft of medications charged to the patient; unrelieved pain or anxiety from receiving a substituted or diluted dose; unintended opioid withdrawal; substandard care and reckless endangerment from impaired healthcare workers; bloodstream infections from adulterated products or contaminated syringes[10,11]; adverse drug or hypersensitivity reactions if patients have been unknowingly provided with medications they should not receive; and inaccurate or falsified documentation in the patient's medical record.

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All of the "-tecans" are available for parenteral administration; however, topotecan is also available as an oral capsule formulation. These drugs are considered hazardous according to the National Institute for Occupational Safety and Health (NIOSH) and require the use of engineering controls (a biologic safety cabinet) and personal protective equipment (PPE) when being handled.

Common side effects associated with "-tecans" include, but are not limited to, gastrointestinal effects, fatigue, and hair loss. Diarrhea is one of the most common gastrointestinal side effects and can be life-threatening. For example, patients who receive irinotecan may have an acute (early) onset of diarrhea that may begin while the drug is being administered, or soon after. Or they may experience delayed onset diarrhea which occurs 24 hours after the drug was administered. Patients should be instructed to purchase loperamide (**IMODIUM**), which is available over-the-counter, to have at home in case diarrhea begins after 24 hours. Once the diarrhea begins, the patient needs to start taking the loperamide. Their healthcare provider should give them specific instructions on how much and how often the loperamide should be taken, which will probably be different than what is on the package label. If early or delayed diarrhea continues for more than 24 hours, the patient should contact their healthcare provider immediately.

Other important monitoring parameters that may require dose modifications include, but are not limited to, complete blood count with differential, signs and symptoms of pulmonary toxicity, hepatic function, hypersensitivity, and infusion site reactions. Evaluate for pregnancy status and hepatitis B virus prior to initiating therapy.

All medications in this class have a boxed warning. Topotecan, irinotecan, and Trodelvy have a boxed warning for the risk of severe myelosuppression. Irinotecan and Trodelvy also have a boxed warning for life-threatening diarrhea. Lastly, Enhertu carries a boxed warning for the risk of both interstitial lung disease and embryofetal toxicity.

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Lack of Recognition

Because of the covert nature of diversion, it may be overlooked and may not be suspected or identified at all if detection systems are not in place.[4] Studies have shown that, while healthcare executives acknowledge that substance use disorder is an issue in healthcare, only 17% believed the problem existed in their own facility.[12] Healthcare workers may fail to report drug diversion out of fear of repercussions, acceptance of diversion as a part of the culture, or lack of education on its impact or knowledge of the resources available for reporting.[4] Drug diversion may not be identified until many patients have been harmed, and even when diversion is suspected, the risk of patient harm may be overlooked.[4,12]

Signs of Diversion

Possible signs of diversion can manifest in a worker's physical appearance, behavior, or work habits and performance.[13-15] These may be the only clues of diversion, so personal observation is vital.[4] Physical signs may include wearing long-sleeved clothing even in warm environments, shakiness, tremors, slurred speech, sweating, bloodshot eyes, appearing visibly intoxicated, or deterioration in one's personal appearance.[15] Behaviors of an employee who may be diverting drugs include increased isolation and social avoidance at work, frequent illnesses or absences from work, frequent trips to the restroom or locker room and other unexplained absences, increased accidents or injuries, refusing drug testing, being unreliable, taking greater effort or more time to complete ordinary tasks, or providing elaborate excuses.[15] Suspicious work habits and performance indicators of a worker who may be diverting drugs include consistently arriving early, staying late, volunteering for overtime, "wasting" controlled substances more often than peers, or transporting/storing controlled substances in their pockets.[13,15] Additional at-risk behaviors worth investigating include unnecessary dilution practices; access to the automated dispensing cabinet (ADC) more than 30 minutes prior to the administration time; removal of larger than required doses, resulting in the need for wasting; removal for a patient not assigned to them; and wasting of complete doses.

Other patterns or trends that may be identified within the organization's medication-use system include frequent incorrect controlled substance counts and discrepancies, increases in usage of controlled substances outside of normal levels, requesting a specific controlled substance, missing medications, signs of tampering with medication packaging, improper storage of controlled substances, frequent overrides in drug dispensing technologies, waste not being appropriately witnessed or large and inconsistent amounts of waste, controlled substances being removed from an unsecured waste container, or expired controlled substances being removed from their holding area.[14,15] Other signs include poor documentation of the chain of custody of controlled substances, which could include late documentation, coworkers habitually helping each other in completing documentation, or inappropriate documentation "batching."[13,15] Additional potential warning signs include leaking intravenous (IV) infusions containing controlled substances, complaints of poor pain management by patients, medical records that demonstrate erratic pain relief, and unexplained transmission of infection.[16]

Up next

Be on the lookout for **Part II** on this topic in an upcoming newsletter, which will discuss tools for preventing, identifying, reporting, and responding to diversion. For further information, please listen to the recording of the following drug diversion webinars: ***Part I: The Pursuit of Prevention—Confronting Drug Diversion*** (www.ismp.org/node/61019) and ***Part II: Reducing the Risk and Infection Outbreaks from Drug Diversion*** (www.ismp.org/node/61022).

References:

1) Nyhus J. Drug diversion in healthcare. American Nurse. 2021;15(5):23-7. Accessed December 13, 2022. www.ismp.org/ext/1058
2) Michalek C, Fortier C, Haumschild R. Prevention of drug diversion in the healthcare setting. Institute for Safe Medication Practices (ISMP) webinar. May 18, 2020. Accessed March 10, 2022. www.ismp.org/node/14862

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SAFETYwire

Smudged IV bag label and a proxy scan set up a patient for a cardiac arrest. A nurse administered heparin instead of norepinephrine to a critical, septic elderly patient. The omission of norepinephrine contributed to severe hypotension and cardiac arrest. The patient had been admitted for the evaluation of a right lower extremity ulceration. Throughout their admission, the patient's renal function, blood pressure, and overall clinical status declined, eventually warranting intubation and continuous renal replacement therapy (CRRT). The patient was also receiving high doses of three vasopressors, including norepinephrine, to maintain adequate blood pressure, as well as a heparin infusion for new-onset atrial fibrillation with a rapid ventricular response.

A smart infusion pump alerted a nurse that the patient's norepinephrine infusion was running low. The nurse requested an infusion of norepinephrine (16 mg/250 mL) as well as heparin (25,000 units/250 mL) from the pharmacy since the heparin infusion was also running low. The pharmacy dispensed both infusions via the pneumatic tube system. The nurse mistakenly brought the heparin infusion bag instead of the norepinephrine bag into the patient's room and hung it on the intravenous (IV) pole directly behind the currently running norepinephrine bag in anticipation of needing to change the bag. The nurse then attempted to scan the barcode on the pharmacy's thermal label affixed to the bag of heparin, thinking it was norepinephrine, but the barcode would not scan because it had been smudged with alcohol-based hand sanitizer. As a workaround, the nurse scanned the bag of norepinephrine currently infusing. The nurse did not further examine the heparin label and administered it at the rate the norepinephrine infusion had been running. Given the patient's critical status along with the omission of norepinephrine, they experienced cardiac arrest. Return of spontaneous circulation was achieved, and the erroneous heparin administration was discovered once the patient was stabilized. However, the patient's clinical status continued to decline, and they died 2 days later.

Investigation of the error led to the identification of several contributing factors,

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3) 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; 2020. Accessed December 14, 2022. www.ismp.org/ext/1061
4) New K. Institutional diversion prevention, detection, and response. Presentation at: National Association of Drug Diversion Investigators (NADDI) Tennessee Chapter Meeting; 2013. Accessed December 15, 2022. www.ismp.org/ext/1067
5) Knight T. Is your organization protected from diversion of high-value drugs? *Healthcare Business Today.* December 9, 2021. Accessed December 14, 2022. www.ismp.org/ext/1068
6) National Association of Drug Diversion Investigators (NADDI). Drug diversion. 2022. Accessed December 19, 2022. www.ismp.org/ext/1059
7) Baldisseri MR. Impaired healthcare professional. *Crit Care Med.* 2007;35(suppl):S106-16.
8) New K. Drug diversion in health care settings can put patients at risk for viral hepatitis. *Minority HIV/AIDS Fund, US Department of Health & Human Services* blog. May 2, 2014. Accessed December 16, 2022. www.ismp.org/ext/1060
9) Invistics. Porter Research study 2020: a comprehensive look at drug diversion from the view of healthcare executives [White paper]. Norcross, GA: Invistics. 2021. Accessed December 15, 2022. www.ismp.org/ext/1066
10) Rosa K. Understanding infectious disease risks associated with drug diversion & how to prevent events. ContagionLive. April 23, 2018. Accessed December 15, 2022. www.ismp.org/ext/1062
11) Eisler P. Doctors, medical staff on drugs put patients at risk. *USA Today.* April 17, 2014. Accessed December 13, 2022. www.ismp.org/ext/1069
12) Tribble DA. How big is the drug diversion problem? Nobody knows! BD. December 2, 2019. Accessed October 11, 2022. www.ismp.org/ext/1005
13) Clark J, Fera T, Fortier C, et al. ASHP guidelines on preventing diversion of controlled substances. *Am J Health Syst Pharm.* 2022;79(24): 2279-306.
14) The Joint Commission (TJC). Drug diversion and impaired health care workers. *Quick Safety.* 2019;(48):1-3. www.ismp.org/ext/1003
15) American Association of Nurse Anesthesiology (AANA). Signs and behaviors associated with substance use disorder and drug diversion. American Association of Nurse Anesthesiology. Accessed October 4, 2022. www.ismp.org/ext/1004
16) New K. The role of security in the prevention, detection and response to drug diversion by healthcare personnel. *J Healthc Prot Manage.* 2016;32(2):33-8.

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Thank you for all you do each and every day!

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including recognition that the heparin infusion with the smudged label and barcode should not have been used; it should have been returned to the pharmacy. Also, when the barcode on the infusion bag would not scan, instead of following a standard process to escalate the concern, the nurse used a proxy scan of the barcode on the previously administered norepinephrine infusion bag to confirm what was thought to be a replacement norepinephrine infusion but was actually a heparin infusion. Similar errors with proxy barcode scanning have been reported, including a case in which a nurse scanned an empty heparin bag that was hanging on a patient's pole instead of the replacement bag, which unknowingly contained **ROP**ivacaine (www.ismp.org/node/19769).

To prevent this type of error, the following recommendations should be considered.

Pharmacy should purchase premixed heparin and norepinephrine infusions, when possible, and require barcode scanning of the manufacturer's barcode before dispensing and administering the product. In addition, the medication labels should be tested to see whether smudging of the label and barcode information is possible, especially since practitioners frequently use alcohol-based sanitizers when handling medications. Never use a medication with a smudged label or barcode. Educate practitioners during orientation and annually thereafter, not to administer a medication with a label that is smudged and unreadable, or if the barcode is smudged, which would render it unscannable.

Develop an escalation process for what to do if a medication barcode will not scan (e.g., contact the pharmacy for immediate help). If a barcode will not scan, never use a proxy scan, such as scanning the barcode on an empty infusion or alternative label that is not on the medication being administered.

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