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ISMP An ECRI Affiliate

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

Inappropriate fentaNYL patch prescriptions at discharge for opioid-naïve, elderly patients

We recently heard from a long-term care (LTC) pharmacy about an increase in the prescribing of transdermal fenta**NYL** patches for elderly patients. In most cases, the pharmacists reviewing the patients' orders determined that the fenta**NYL** patches had been inappropriately prescribed for opioid-naïve patients, sometimes to treat acute pain rather than chronic pain. In several cases, the fenta**NYL** patches had been prescribed because of a documented allergy to another analgesic, such as codeine. However, further investigation showed that the "allergy" was a minor intolerance to the analgesic, usually gastrointestinal, such as mild nausea or constipation. The more common underlying cause of prescribing fenta**NYL** patches inappropriately appears to be a knowledge deficit about the dangers of prescribing this potent opioid analgesic to opioid-naïve patients. Several of these events began in a hospital, with opioid-naïve patients receiving prescriptions for fenta**NYL** patches after treatment in an emergency department (ED) or upon discharge and transfer to a LTC facility. ISMP has written about this well known problem for decades. Since it is STILL an ongoing problem, it is time to revisit this issue.

Background

In 1990, **DURAGESIC** (fenta**NYL** transdermal system) was approved by the US Food and Drug Administration (FDA). Years later, generic fenta**NYL** patches became available. As early as 2005, FDA published a public health advisory and information for healthcare professionals regarding the appropriate and safe use of the fenta**NYL** transdermal system, noting that serious, life-threatening, or fatal respiratory depression may occur.[1] FDA followed up with another advisory in 2007, stressing that transdermal fenta**NYL** is *only* indicated for use in patients who are opioid-tolerant with documented chronic, moderate-to-severe pain.[2]

Today, the official prescribing information recommends use of fenta**NYL** patches only in opioid-tolerant patients for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. According to the prescribing information, patients considered opioid-tolerant are those taking, for 1 week or longer, at least:

- 60 mg of oral morphine per day
- 60 mg of oral **HYDRO**codone per day
- 30 mg of oral oxy**CODONE** per day
- 25 mg of oral oxy**MOR**phone per day
- 8 mg of oral **HYDRO**morphone per day
- 25 mcg of transdermal fenta**NYL** per hour
- An equianalgesic dose of another opioid

In addition, in 2012, FDA approved an extended-release (ER) and long-acting (LA) opioid analgesic Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of prescribing ER and LA opioids, including fenta**NYL** patches, outweigh the risks.[3] In 2018, that REMS was modified to reduce the risk of abuse, misuse, addiction, overdose, and deaths due to all prescription opioid analgesics.[4] The REMS strongly encourages specific training about the risks and safe use of opioids for all healthcare providers involved in

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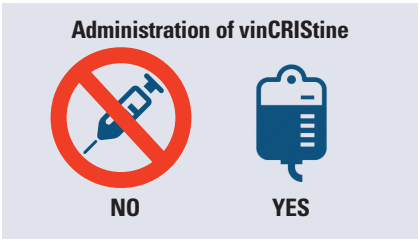
REMINDER

HIGH-ALERT

Time to end vinCRIStine syringe administration. In case you missed the announcement in our last newsletter, the US Food and Drug Administration (FDA) and Pfizer have removed wording from the vin**CRIS**tine package insert that described direct intravenous (IV) injection of vin**CRIS**tine via a syringe (FDA removes syringe administration from vin**CRIS**tine labeling. *ISMP Medication Safety Alert!* June 18, 2020; www.ismp.org/node/18548). The **WARNINGS** section of the package insert now states, **"To reduce the potential for fatal medication errors due to incorrect route of administration, vinCRIStine sulfate injection should be diluted in a flexible plastic container and prominently labeled as indicated "FOR INTRAVENOUS USE ONLY—FATAL IF GIVEN BY OTHER ROUTES."**



More than 140 deaths are known to have occurred in the US and globally due to accidental intrathecal injection of the drug via syringe, often when it was mixed up with, or wrongly assumed it was supposed to be given with, another drug meant for intrathecal administration, such as methotrexate. No such cases have been reported with dilution of vin**CRIS**tine in a minibag, due to physical differences in the packaging and the need for an administration set. Unfortunately, some practice sites are still using syringes to administer IV vin**CRIS**tine. Based on data collected in response to the ***ISMP Medication Safety Self Assessment for High Alert Medications*** between September 2017 and March 2018 from 442 US hospitals, nearly 20% of respondents still used syringes at least

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the management of patients with acute or chronic pain. FDA believes that, with training, the proper analgesic will be selected for the patient and used with appropriate clinical oversight and monitoring. The agency has even created a blueprint to specify the content of an opioid educational program for healthcare providers.[5] However, there is no mandatory federal requirement for REMS-compliant education about opioids, including fenta**NYL** patches, as a precondition to prescribing, as FDA concluded that monitoring compliance would be unduly burdensome.

Inappropriate prescribing of fentaNYL patches

The LTC pharmacy that reported the rise in inappropriate prescribing of fenta**NYL** patches provided numerous examples, three of which originated in hospitals and are described below. Again, most of these events demonstrated the prescribers' lack of knowledge about avoiding this analgesic in opioid-naïve patients and/or an inaccurate classification of a drug intolerance as an allergy. Prescribing a fenta**NYL** patch to elderly, opioid-naïve patients can result in fatal or life-threatening respiratory depression and overdose. Additionally, with the elderly population, there are a number of risk factors, including age-related comorbidities, polypharmacy, and drug-drug interactions, that can further contribute to an unintentional overdose if opioids are inappropriately prescribed.

Event ①

*An 88-year-old resident from a LTC facility fell and was taken to a local hospital ED, where multiple rib fractures were diagnosed. Upon discharge from the ED, the resident was prescribed a transdermal fenta**NYL** patch, 25 mcg/hour, every 72 hours. When the resident returned to the LTC facility, a consultant pharmacist reviewed the medication orders. Looking at the resident's medication history, the pharmacist determined that the resident had not received a prescription for opioids in the past year, revealing he was opioid-naïve. The consultant pharmacist contacted the prescribing ED physician to discuss the order for the fenta**NYL** patch. The ED physician reported that the resident had received "3 small IV push doses" of fenta**NYL** in the ED, mistakenly believing this to mean the resident was opioid-tolerant.*

*Additionally, the ED physician had prescribed the fenta**NYL** patch because the resident had a documented allergy to codeine. Thus, the ED physician mistakenly believed the fenta**NYL** patch was the only viable option. The consultant pharmacist clarified that the LTC records indicated that the resident had experienced mild nausea and stomach upset while taking **HYDRO**codone and acetaminophen (**VICODIN**) when he was younger, which is not an allergy but rather a mild intolerance. The ED physician changed the resident's analgesic to oral oxy**CODONE** 5 mg as needed every 4 to 6 hours.*

Event ②

*An 85-year-old hospitalized patient with persistent pain from a recent fall was discharged with orders for **HYDRO**morphone 1 mg by mouth every 4 hours as needed for pain, which he had received during his 3-day hospitalization. Before the patient was transferred to a LTC facility, the physician also prescribed a 50 mcg/hour fenta**NYL** patch to be applied at discharge for pain management. When reviewing the transfer orders, a LTC pharmacist noticed that the patient did not have a history of taking opioids prior to his 3-day hospitalization and was concerned about the fenta**NYL** patch that had been applied prior to transfer, particularly in combination with the prescribed **HYDRO**morphone. The pharmacist contacted the LTC physician, who initially did not want to discontinue the fenta**NYL** patch since it had been recommended by the hospital physician. The pharmacist was persistent and convinced the LTC physician that the fenta**NYL** patch was unsafe in the elderly, opioid-naïve patient. The patch was removed and discarded.*

Event ③

*A 65-year-old patient with back pain had been taking **HYDRO**codone with acetaminophen 5 mg/325 mg once or twice daily for the past week. When he was hospitalized for a*

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part of the time, including 13% who always used syringes to administer IV vin**CRIS**tine. Thus, the risk of accidental intrathecal injection still exists in the US and globally.

Dispensing vin**CRIS**tine and other vinca alkaloids in a minibag of compatible solution, and not in a syringe, was among the very first ISMP ***Targeted Medication Safety Best Practices for Hospitals*** (www.ismp.org/node/160), which were launched in 2014. Then, in March 2019, ISMP called on the FDA to eliminate all mention of syringe administration from official vin**CRIS**tine labeling (www.ismp.org/node/1492).

ISMP has frequently referred to wrong route administration of vin**CRIS**tine and vinca alkaloids as the "most serious of all medication errors." Patients experience tremendous pain and are often aware of their impending death, which typically occurs within days or weeks. There is no effective reversal once the mistake is made. Even with the labeling change, there is nothing to stop healthcare practitioners from administering vin**CRIS**tine via syringe (except if they can only get the drug dispensed in a minibag). We hope that every hospital and health system will investigate exactly how vin**CRIS**tine is being administered at any site that uses the drug. It is time to end the practice of syringe administration by making it a requirement for all vin**CRIS**tine doses to be diluted in a minibag.

SAFETY briefs

Letting the docs dispense. A recent editorial in *The Wall Street Journal* roused some concerns when the authors suggested that, "instead of forcing patients to stand in line at a drugstore to fill their prescriptions, it would be easier and cheaper if these patients could get their meds directly from the doctors prescribing them" (www.ismp.org/ext/506). The editorial provided commentary about a lawsuit by 3 doctors in Montana who are seeking the freedom to dispense "non-controlled medications directly to their patients at cost," which is currently banned in their state. The editorial said the ban was less about protecting patients and more about protecting a middleman from competition.

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*different reason, he mentioned taking this oral analgesic periodically for back pain when asked about his medication history. The patient was concerned that his back pain would worsen during hospitalization and asked the nurse if he could try a "pain relieving narcotic patch." The nurse documented this request. When the patient was discharged the next day to a LTC facility for rehabilitation, the physician noticed the patient's request to try a "pain relieving narcotic patch" and prescribed a fenta**NYL** patch 25 mcg/hour every 72 hours for back pain, which he included on the patient's transfer orders. A LTC pharmacist reviewing the transfer orders contacted the prescriber, who stated that the patient did not want to take analgesic tablets any longer and had personally requested the patch. Through further discussion with the pharmacist, the prescriber realized the patient was not an appropriate candidate for a fenta**NYL** patch and instead ordered oral **HYDRO**codone with acetaminophen 5 mg/325 mg every 4-6 hours for back pain.*

Recommendations

ISMP is concerned about these and other reports of inappropriate prescribing of fenta**NYL** patches for opioid-naïve, elderly patients. Fenta**NYL** patches should only be prescribed for patients who are opioid-tolerant with persistent, moderate-to-severe chronic pain that requires around-the-clock, long-term opioid administration. This is so critical to safety that, in 2018, ISMP called for the elimination of prescribing fenta**NYL** patches for opioid-naïve patients and/or patients with acute pain in our ***Targeted Medication Safety Best Practices for Hospitals*** (www.ismp.org/node/160). In 2020, this Best Practice was incorporated into a new Best Practice (#15) to verify and document the patient's opioid status and type of pain before prescribing and dispensing ER or LA opioids.

The most recent stream of reports, some of which are described above, are closely associated with a knowledge deficit about pain management and proper prescribing of fenta**NYL** patches. These examples and others help substantiate the fact that reliance on product labeling and practitioner education alone will not do enough to solve this life-threatening problem. Yes, prescribers should be educated about safe fenta**NYL** patch prescribing, and their competency should be verified as a prerequisite to prescribing this potent opioid. However, education alone is a weak safety strategy (www.ismp.org/node/18343), and there will always be some who are unaware of the great risks they take when prescribing fenta**NYL** patches to opioid-naïve patients to treat acute pain. Thus, system safeguards must be established for this high-alert medication to avoid the risk of harm.

The examples of inappropriate prescribing of fenta**NYL** patches described above occurred upon transfer to a LTC facility. Thus, our typical recommendations alone to improve proper inpatient prescribing (e.g., automatic interchange, pharmacy interventions with prescribers), safe storage only in clinical locations where chronic pain is primarily treated, and mandatory discharge and ambulatory patient education, may not be enough to reduce the risk of inappropriate prescriptions upon transfer. While all of these instances of inappropriate prescribing were thankfully detected by LTC pharmacists *after* patients had been transferred to a LTC facility, thus preventing serious patient harm, additional strategies *before* these transitions in care should be implemented in the hospital.

For example, when entering discharge and transfer orders, interactive alerts requiring confirmation that the patient is opioid-tolerant and experiencing chronic pain might help prevent inappropriate prescribing, as might hard stops if patients do not meet prescribing criteria, including in the ED. Also consider creating a daily list of discharge prescriptions and transfer orders for fenta**NYL** patches generated from the order entry system, and requiring a hospital pharmacist to review the orders and prescriptions to verify that the patient is opioid-tolerant and has chronic pain.

In addition, distinguishing between true allergies and drug intolerances is critical to the proper selection of analgesics. When allergy information is collected, include prompts to obtain and document in a standardized manner the reaction type (e.g., side effect, intolerance, toxicity, immune response) and description (e.g., rash, pruritus, swelling,

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Years ago, a similar suit by a group of oncologists in Utah inspired ISMP to examine the practice of physician dispensing, and we took a position on the practice that was published in our March 8, 2012 newsletter (www.ismp.org/node/698). In that article, we stated that we "fully support the removal of any barriers to patients' access to medications, cost containment that can be achieved by the use of lower-cost but effective medications, and steps that improve patient adherence to prescribed medication therapy." However, we also stated unequivocally that we cannot support "unbridled" physician dispensing due to the increased risk of medication errors, particularly with high-alert medications such as chemotherapy.

What cannot easily be dismissed are the potential safety issues with physician dispensing, such as bypassing safety alerts issued during order entry with clinical decision support; labeling and packaging issues; the potential for conflict of interest where a profit motive may exist (rare, and not the case in the Montana lawsuit); and availability of third-party reimbursement. From a patient safety standpoint, ISMP cannot support physician dispensing at this time since the process has not been well-thought out, does not incorporate critical safety measures to protect against medication errors, and there is no regulatory oversight.

Nymalize oral syringes to be adapted for ENFit. As mentioned in our May 21, 2020 newsletter, Arbor Pharmaceuticals has made changes to **NYMALIZE** (ni**MOD**ipine) oral solution, including a change in concentration from 3 mg to 6 mg per mL, availability only in a prefilled oral syringe, and discontinuation of unit dose cups and a 473 mL (pint) bottle. Providing the medication solely in prefilled oral syringes led to concerns from hospitals that have converted to ENFit tubing, which is not compatible with oral syringes.

ISMP discussed the situation with Arbor and the US Food and Drug Administration (FDA). We learned last week that the company is working on both short- and long-term solutions for hospitals that use ENFit. Arbor said the company is in the process

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anaphylaxis). Before prescribing medications, allergy information without a documented reaction type and description should be reconciled with the patient or caregiver so crucial medications are not avoided simply due to mild intolerances.

References

1) FDA. Important information for the safe use of fentanyl transdermal system (patch). Public Health Advisory and Information. July 2005. Contents archived.
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3) FDA. Extended-release (ER) and long-acting (LA) opioid analgesics risk evaluation and mitigation strategy (REMS). Approved July 2012, updated June 2015. www.ismp.org/ext/508
4) FDA. Opioid analgesic risk evaluation and mitigation strategy (REMS). September 27, 2018. www.ismp.org/ext/509
5) FDA. FDA's opioid analgesic REMS education blueprint for health care providers involved in the treatment and monitoring of patients with pain. September 2018. www.ismp.org/ext/510

Update on Omnicell variable character search feature

As we have seen repeatedly, problems can occur with automated dispensing cabinet (ADC) drug name searches when just 2 or 3 characters are typed to select medications via override or from a non-profiled cabinet. This problem was illustrated most recently in our May 14, 2020, issue (www.ismp.org/node/17746) when a patient received verapamil instead of **VERSED** (a former brand of midazolam). A nurse used the cabinet override feature to select and access the drug "Versed" by entering the first few letters of the drug name. However, she accidentally selected and removed a vial of verapamil (5 mg/2 mL) from the ADC, which was available via override. Verapamil was then administered to the patient by IV push. The incident was strikingly similar to an earlier tragic error in which a patient died after receiving vecuronium instead of Versed after entering just "V-E" in the drug name search field (www.ismp.org/node/1326).

Searching drug names using just 1, 2, or 3 letters can lead to these situations, which is why we have recommended using at least 5 letters when searching for a drug in electronic systems. In the 2019 article cited above, we called upon ADC vendors to consider software changes to allow a configurable option for the required number of letters to narrow the choices, ideally to one drug or drug category. So far, we only know of Omnicell having such a feature (in the Omnicell XT ADCs), although BD/Pyxis has promised enhancements soon as well.

We recently learned a little more about how the Omnicell function works. The character search configuration is at the cabinet level and not at the individual drug item level. There is a series of tabs for clinicians to select the category of medication being removed, such as "Scheduled Meds," "Active Med Orders," "PRN Only," and "Stocked Meds." "Stocked Meds" is where the override function resides. If nurses access a medication via override, the cabinet can be set to address safety so that at least 5 letter characters must be entered to select a drug (**Figure 1**). The search functionality under "Scheduled Meds," "Active Med Orders," and "PRN Only" was not changed, so these do not require a 5-character search. Only medication searches for drugs obtained via override ("Stocked Meds") require a 5-character search. Requiring a 5-character search for scheduled, active, and PRN medications may cause frustration and may not be required, as only medications prescribed and verified for the patient will appear during these drug name searches. We hope those who have Omnicell XT ADCs will make sure this important feature is set to require a 5-character search for drugs obtained via override.

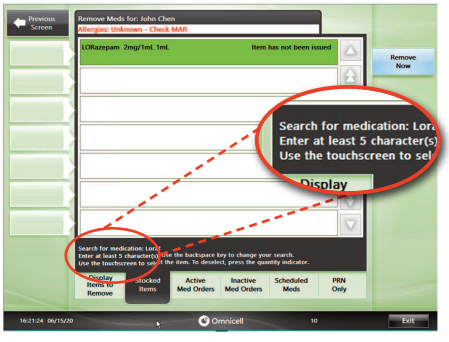

Figure 1. With Omnicell XT ADCs, stocked items obtained via override require the entry of at least 5 characters during searches.

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of testing an adapter for the oral syringe that it believes will be a short-term solution to the compatibility issue. Provided that study results are positive, the company said it will be able to offer customers the new adapter in the near future at no additional cost. Stay tuned for more information.

Special Announcements

ISMP survey on Best Practices open

There are still 2 weeks left to take our survey on the level of implementation of the two new ***2020-2021 Targeted Medication Safety Best Practices*** (TMSBPs) ***for Hospitals***. Since we are only conducting the survey on the two new Best Practices, it should only take you about 5 minutes. The survey is available at: www.ismp.org/ext/350 and will be open through **July 17, 2020**.

Accepting CHEERS AWARDS nominations

Nominations for this year's ISMP CHEERS AWARDS will be accepted through **September 11, 2020**. The prestigious AWARDS celebrate the efforts of individuals, organizations, and groups that have demonstrated an exemplary commitment to medication safety. The winners will receive the AWARD in early **December**—more to follow. To submit a nomination, visit: www.ismp.org/node/1036. ISMP accepts external nominations, including self-nominations.

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