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ISMP
An ECRI Affiliate

Community/Ambulatory Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Multiple NDCs for a single prescription fill leads to overdose

Problem: A patient was recently admitted to the hospital with kidney failure as a result of taking a high dose of the urinary analgesic phenazopyridine. The patient had been prescribed phenazopyridine 200 mg with instructions to take one tablet three times a day. However, instead they took 2 tablets (400 mg total) three times a day after being confused by how the pharmacy dispensed the medication.

To fill the patient's prescription, the pharmacy used phenazopyridine from two different manufacturers (i.e., two different national drug codes [NDCs]). They dispensed some tablets from one manufacturer in the first prescription vial and the remainder of the tablets from a different manufacturer in a second prescription vial. At the point of sale, the patient did not receive counseling that explained the dispensing of two vials or instructions to take tablets from only one prescription vial until it was empty and then continue with the other prescription vial. As a result, the patient took one tablet from each prescription vial for each dose resulting in the overdose.

From time to time, pharmacies purchase medications from different manufacturers resulting in multiple brands of the same generic formulation available for use. They may do this when a specific manufacturer's product is no longer available or when they are able to purchase the product from a different manufacturer (i.e., a different NDC) for a lower cost. In either scenario, pharmacies will often try to dispense any remaining quantity of the original manufacturer's products (i.e., original NDC) to use up the remaining inventory. To help accomplish this, some pharmacies may choose to dispense two different NDCs for a single prescription. As in the case reported above, pharmacists may dispense two different NDCs in two different prescription vials. ISMP is also aware of pharmacies that dispense two different NDCs in the same prescription vial separated by cotton.

With either the one- or two-prescription vial method to dispense multiple NDCs at a time, medication safety risks are introduced. Barcode scanning of the second NDC dispensed may not be possible, and perpetual inventory of this second NDC may likely need to be manually adjusted. Also, in cases when only a single NDC can be entered for a prescription, the prescription label may not reflect the medication contained in the prescription bottle and thus be mislabeled. Pharmacist product verification also may be compromised; for example, the electronic tools (e.g., barcode scanning during fulfillment, display of the product image during verification) to help inform the verification process may not be available for the second NDC dispensed. In addition, if the pharmacy computer system can only submit a claim for one NDC, yet two NDCs are dispensed, insurance companies may consider this fraudulent billing practice. And, of course, dispensing multiple NDCs for a single prescription fill can lead to patient confusion, dosing errors, and patient harm, as evidenced by the case described earlier.

Safe Practice Recommendations: When possible, dispense only one NDC for a prescription at a time. If the pharmacy does not have enough medication to dispense the entire prescription using one NDC, discuss alternative options with the patient, including:

- If a stock replenishment order is expected, assess the patient's supply to determine if they have enough doses to wait until the refill can be processed using the same NDC. Otherwise, provide the patient with sufficient medication to last until the pharmacy order arrives.

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Look-alike Sandoz ophthalmic cartons. A pharmacist reported the potential for wrong-drug errors involving cyclopentolate ophthalmic solution and tropicamide ophthalmic solution, both marketed by Sandoz. The cartons for both products look almost identical (**Figure 1**). Each are the same size, use the same font and font size for the drug name, contain the strength (i.e., 1%) in white lettering with a red background, and display the same manufacturer trade dress at the bottom of the principal display panel.

Figure 1. Cartons of cyclopentolate (left) and tropicamide (right) ophthalmic solutions from Sandoz appear nearly identical.

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

Items from the **September – December 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 as an Excel file here.

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- Discuss the possibility of transferring the prescription to another pharmacy within the system (or an unaffiliated pharmacy) that has enough quantity.

Alternatively, determine if there are pharmacy computer system enhancements available that would allow the pharmacy to dispense, accurately label, and bill for two separate NDCs for one prescription fill. For example, one pharmacy shared during a recent Medication Safety Officers Society (MSOS) *Briefing* webinar that their pharmacy computer system allows them to essentially fill a prescription twice, first as a partial fill with one NDC and then process the remainder as a second fill with a different NDC to complete the prescription at the same time of dispensing. In other words, the pharmacy can dispense and adjudicate each NDC used for the partial fills for the same prescription fill.

In their workflow, when the prescription requiring two NDCs is processed, the pharmacy technician selects the first NDC to be used, checks "Partial Fill" in the dispensing system, fills the first part of the prescription using barcode scanning, affixes a label for that NDC to the prescription vial, and routes it to the pharmacist for verification. The pharmacist, due to the selection of the "Partial Fill" box by the technician, is alerted that the prescription is a partial fill. The pharmacist verifies the partial fill and applies a sticker indicating that the bottle is 1 of 2. The pharmacist is then prompted to select the second NDC to be used to complete the prescription fill. Once the drug is selected from the pharmacy shelf, the prescription is passed back to the pharmacy technician who fills the remainder of the prescription, using a second vial, with the second NDC and affixes a prescription label specific for that NDC to the second vial. The full prescription (both prescription vials) is handed off to the pharmacist for verification and a 2 of 2 sticker is added to the second prescription vial. The two prescription vials are placed in a separate bag from other prescriptions being filled for the patient and the prescription is flagged within the pharmacy computer system for mandatory patient education.

Additionally, to help prevent potential patient confusion, the pharmacy limits the filling of a prescription with two NDCs to patients who are already taking the medication. For new therapies, medications dispensed as part of their Meds2Beds program, and patients with cognitive barriers who may be confused by having two prescription vials for the same drug, the pharmacy takes steps to dispense the prescription using only a single NDC. In addition, this pharmacy will not dispense multiple partially filled prescriptions to the same patient at the same time.

After determining your standard work, ensure your dispensing workflow and practices comply with insurance and state and federal pharmacy regulations. Avoid practices that will result in mislabeling of the prescription vial. Create and/or update policies and job aids to help staff comply with the established workflow.

Patient education, using the teach-back method, is critical when multiple NDCs are dispensed for a single prescription to ensure patients understand how and when to take their prescribed medication(s). Establish a system to ensure patients receive education. Electronic hard stops at the point of sale can be utilized to restrict completion of the sale until patient education has occurred.

Special Announcement

ISMP survey on parenteral nutrition (PN)

We are conducting a short survey about PN including the use and safety of multi-chamber bag parenteral nutrition (MCB-PN) and patient-specific compounded (i.e., custom) PN. Please take 10 minutes to complete this survey by **January 23, 2025**. We appreciate your participation!

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One strategy to prevent mix-ups is to purchase products from different manufacturers to reduce the number of look-alike containers. Storing ophthalmic products intermingled with the rest of the pharmacy inventory, rather than segregating them in their own section, might be of benefit. Thankfully, given the names start with either "c" or "t," it is less likely they will be stored next to one another alphabetically on a pharmacy shelf. Barcode scanning prior to dispensing is a must to prevent errors from reaching patients. The US Food and Drug Administration (FDA) should work with manufacturers to reduce similarity among look-alike containers.

Reconstitution error with Shingrix vaccine. In previous ***Safety briefs***, we discussed errors in which only a single component (adjuvant suspension or lyophilized powder) of **SHINGRIX** (zoster vaccine recombinant, adjuvanted) has been administered instead of both components. However, errors involving Shingrix continue to be reported through the ***ISMP National Vaccine Errors Reporting Program*** (ISMP VERP). Recently, we learned that another practitioner mistakenly administered only the Shingrix adjuvant suspension component. As a result, the patient had to come back to the clinic to receive the full vaccine.

A system should be employed to ensure the Shingrix lyophilized component and adjuvant suspension component vials are stored together to reduce the risk of administering only the diluent or using a diluent from another vaccine. Implement barcode scanning prior to preparing and administering a vaccine. Configure the system to require scanning of both the vaccine and corresponding diluent barcodes.

Potential to confuse KlonoPIN for cloZAPine. A behavioral health practitioner was collecting a patient's medication history. During the conversation, the patient shared that they were recently diagnosed with anxiety and prescribed the benzodiazepine **KLONOPIN** (clonaze**PAM**). However, the practitioner heard clo**ZAP**ine, a second generation (atypical) antipsychotic. Thankfully, they realized that this was not

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Wrong-dose errors are possible with Trikafta packaging

Problem: TRIKAFTA (elexacaftor, tezacaftor, and ivacaftor) is indicated for the treatment of cystic fibrosis (CF) in patients 2 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or a mutation in the CFTR gene that is responsive based on in vitro data. ISMP has received multiple reports of concern that wrong-dose errors related to the packaging of Trikafta can occur when patients require alternative dosing due to moderate hepatic impairment or concomitant use of moderate and/or strong CYP3A inhibitors.

Trikafta is currently available in four carton configurations designed to accommodate normal dosing recommendations. Each configuration contains wallets with either packets of oral granules or tablets. For example, for patients 12 years and older, Trikafta is available in a carton holding 84 tablets contained in 4 wallet (i.e., blister) cards. Each wallet (**Figure 1**) contains 14 fixed-dose combination tablets (elexacaftor 100 mg, tezacaftor 50 mg, and ivacaftor 75 mg) and 7 ivacaftor 150 mg tablets. The dose, administered twice a day, is 2 tablets of elexacaftor 100 mg, tezacaftor 50 mg, ivacaftor 75 mg (total dose of elexacaftor 200 mg, tezacaftor 100 mg, ivacaftor 150 mg) in the morning and 1 tablet of ivacaftor (150 mg) in the evening.

Figure 1. A wallet card of Trikafta. Each wallet contains 14 fixed-dose combination tablets (elexacaftor 100 mg, tezacaftor 50 mg, and ivacaftor 75 mg) and 7 ivacaftor 150 mg tablets. When patients require alternative dosing, not all of the tablets will be taken, introducing the risk of wrong-dose errors.

However, if a patient 12 years and older has moderate hepatic impairment, they should alternate taking 2 tablets of elexacaftor 100 mg, tezacaftor 50 mg, ivacaftor 75 mg in the morning on one day and then only 1 of these fixed-dose combination tablets in the morning the next day. No evening ivacaftor tablet dose is indicated for these patients. This introduces the risk that the patient may take the wrong tablet(s) or extra morning or evening tablets as there will be tablets in each wallet that should not be ingested.

This reminds us of the error-prone situation with the original packaging of **PAXLOVID** (nirmatrelvir and ritonavir) tablets, which is used to treat coronavirus disease 2019 (COVID-19). At the time of the initial emergency use authorization, Paxlovid was only available in a carton holding 30 tablets contained in 5 daily-dose blister cards. Each blister card contained 4 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each). The dose for patients with normal renal function (estimated glomerular filtration rate [eGFR] equal to or greater than 90 mL/minute) or mild renal impairment (eGFR below 90 mL/minute but more than or equal to 60 mL/minute), was 2 tablets of nirmatrelvir (150 mg each, 300 mg total) and 1 tablet of ritonavir (100 mg), administered twice a day, in the morning and evening. However, patients with moderate renal impairment (eGFR below 60 mL/minute, but more than or equal to 30 mL/minute) were to take only 1 tablet of nirmatrelvir (150 mg) along with 1 tablet of ritonavir (100 mg) together, twice daily.

Both ISMP and the US Food and Drug Administration (FDA) received numerous reports of wrong-dose errors related to the original Paxlovid packaging. In one case reported to ISMP, a patient diagnosed with moderate renal impairment and COVID-19 was admitted to the hospital. The admitting physician

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an appropriate drug to treat anxiety and clarified that the patient said Klono**PIN**.

Ensure practitioners are aware of the risk of confusion between these drug names. Please note that the risk for mix-ups between these drug names may be increased in behavioral health settings where both medications may be regularly prescribed. Reinforce with practitioners the need to include and confirm the purpose of the medication in both verbal and written communication.

Wrong delivery address for specialty pharmacy order. A specialty medication was to be delivered to the patient on a Monday. When the patient did not receive the medication as promised, they contacted the pharmacy. Upon investigation, the pharmacy discovered that the package had been delivered to an address a couple blocks away from the correct location. The shipping address had been entered incorrectly with one number being wrong. The pharmacy was able to retrieve the unopened shipping container and deliver the correct medication to the correct patient.

It is important to have processes in place to verify the correct shipping address is being used for each delivery. To help accomplish this, consider having staff ask the patient for their shipping address at the beginning of the call or encounter. Then, that same staff member should read back the address, sounding out each digit, to the patient. If a patient moves or is no longer at an address, the old address should be deleted from the patient's profile, and their preferred shipping address should be updated to prevent shipping the medication to the outdated address. If the patient submits a request online, or via a mobile application, for the medication to be shipped to them, the system should require the patient to enter and/or confirm the address to which the medication should be delivered. Finally, make the patient's current address visible in software systems, on shipping material, and/or on shipping dashboards.

HIGH-ALERT **Double trouble from Camber again – similar drug names and labels.** We have received multiple reports that the 100-count

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ordered to continue administering the Paxlovid blister packages from home. The medication was brought to the pharmacy for identification. The pharmacist identified the medication but realized that the missing tablets did not match the patient's instructions to take one ritonavir and one nirmatrelvir orally, twice a day, which is the correct dose for patients with moderate renal impairment. Although labels were affixed over missing nirmatrelvir tablets on each blister card, which had been correctly removed, there were also missing ritonavir tablets that should not have been removed and some remaining nirmatrelvir tablets that should have been removed from the blisters.

Safe Practice Recommendations: To help patients avoid dosing errors with Trikafta, require pharmacists to counsel them on how to take Trikafta for their prescribed dose. Create a forcing function (e.g., electronic stop in the sales register that requires intervention and acknowledgement by a pharmacist) or mark the prescription receipt to ensure the required counseling is provided. It is extremely important to use the teach-back method, making sure that patients can demonstrate how they will take the morning and evening doses. Show patients how the medication is labeled and packaged in a wallet, and teach them about the different tablets that they should take for each dose. Encourage them to remove each tablet just prior to taking the dose and not ahead of time (e.g., transferring them to a medication box).

Ask patients about any changes in hepatic function, conditions, and other medications they are taking. For situations when patients require alternate dosing, pharmacies should consider implementing a standard procedure for pharmacy staff to apply auxiliary labels or otherwise indicate on each wallet which tablets should be taken for each dose (and which should not be taken). In consultation with patients, pharmacists may also consider removing unnecessary tablets or granule packets. Ideally, there should be separately available packaging to accommodate the recommended alternate dosing regimens, along with a specific set of clear instructions for patient use.

We have shared our concerns and recommendations with the FDA and the manufacturer. If you learn of medication errors potentially related to Trikafta, report them to the ***ISMP National Medication Errors Reporting Program*** (ISMP MERP).

Worth repeating...

Standardize the process to reconstitute oral products

We have once again received an error report describing a situation in which a parent picked up an antibiotic for their child which was not reconstituted. The child was ordered clindamycin oral solution. It was not until the parent arrived home that they realized the medication had not been reconstituted by the pharmacy. Thankfully, they realized the error and did not administer the powder, which has happened in other reports we have received.

It is critical that pharmacies standardize the process used to prepare and dispense oral suspensions and solutions that require reconstitution. Incorporate technology at the point of sale that alerts pharmacy staff that the prescription needs to be reconstituted. Explore options to have the alert be interactive, requiring the staff person to confirm that the medication has been reconstituted. Add a distinct visual cue to the prescription receipt indicating that the medication needs to be reconstituted prior to dispensing. Do not place the actual product container that requires reconstitution in the same bag with other prescriptions for the patient. Establish a process to verify that the correct amount of liquid has been measured and used to reconstitute the drug. After the product is reconstituted, the product should be given to the pharmacist to counsel the patient on how to measure the medication. Open the bottle with the patient or caregiver to check that the contents have been reconstituted. Use the teach-back method when educating patients. Have the caregiver or patient demonstrate how they will measure and administer the dose to validate comprehension. Ensure that an appropriate metric-only dosing device, which corresponds to the instructions on the label, is provided with the prescription.

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bottles of oxy**CODONE** and acetaminophen 5 mg/325 mg and **HYDRO**codone and acetaminophen 5 mg/325 mg tablets manufactured by Camber Pharmaceuticals look very similar with their stylized labels (**Figure 1**). For example, the company name is placed at the top of both labels (rather than the drug names). Also, vertical yellow stripes on the left side of the label and yellow color patterns for the dosage strength background make the bottles look almost identical.

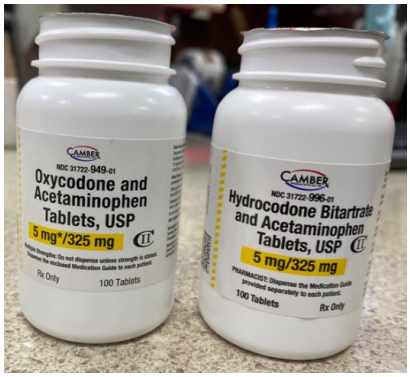

Figure 1. Look-alike bottles of oxy**CODONE** and acetaminophen (left), and **HYDRO**codone and acetaminophen (right) from Camber Pharmaceuticals.

What makes a mix-up even more likely is that the two drug names also look similar; both products contain acetaminophen, and both are used to treat pain. In fact, ISMP has received several reports of mix-ups between these drug names. Barcode scanning will help prevent mix-ups, but we would also recommend purchasing one of these drugs from a different manufacturer so the bottles look different. We have notified the manufacturer of this look-alike issue.

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