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ISMP An ECRI Affiliate

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

Screening for dihydropyrimidine dehydrogenase (DPD) deficiency in fluorouracil patients: Why not?

ISMP is aware of several reports of patients who suffered severe toxicities or even death from the fluoropyrimidine chemotherapy drugs, fluorouracil and capecitabine (**XELODA**), an oral prodrug that is metabolized to fluorouracil after ingestion. These patients had a genetic condition called dihydropyrimidine dehydrogenase (DPD) deficiency, a diagnosis that neither the patients nor their doctors were aware of until it was too late. The DPD enzyme is critical for the metabolism of fluoropyrimidine drugs. With deficient enzyme function, patients can experience severe toxicities with standard doses of fluoropyrimidine chemotherapy.[1] While the incidence of DPD deficiency is relatively low, ranging from 1 to 7 percent of the population depending on ancestry,[2] the consequences are potentially fatal.

Recent Event

A recently reported case involved a patient with breast cancer who was prescribed capecitabine. Within the first week of treatment, she began to develop mild drug-related symptoms including fatigue, weight loss, loss of appetite, and diarrhea. By the second week, her symptoms worsened, including mucositis, hand-foot syndrome (skin reaction caused by leakage of the chemotherapy through capillaries in the palms of the hands and soles of the feet), extreme weight loss, fatigue, diarrhea, and a cough. After completing her first 2 weeks of therapy, she had become so weak that she required hospitalization. After hospitalization, her symptoms continued to worsen, including hand and foot desquamation, severe mucositis, dry eyes requiring artificial tears, delirium, and prolonged leukopenia. Her mouth, lips, throat, and esophagus were covered with lesions and blood. Her hair was falling out. Eventually she became unresponsive. Only later was it found that she had a DPD deficiency, so her body was unable to clear the capecitabine. She died just one month after starting therapy.

ISMP was heartbroken to learn about this preventable death, as a DPD deficiency can be detected through genetic testing prior to starting fluoropyrimidine chemotherapy. Having this information beforehand allows providers to preemptively reduce the dose of the patient's therapy and mitigate potential toxicities, or not give therapy at all if the patient is totally deficient, as no fluorouracil dose has been proven safe for patients with complete absence of DPD activity.

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Deadline for new assessment extended to October 1, 2021!

We have extended the deadline to submit your findings to us for the ***ISMP Medication Safety Self Assessment® for Perioperative Settings*** until **October 1, 2021**. If you are a US hospital that offers perioperative services, a freestanding ambulatory surgery center (ASC), or another facility that offers medical and/or surgical procedures under sedation, we encourage you to take this opportunity to complete the assessment tool. Also, facilities can listen to a **FREE** recorded webinar (www.ismp.org/node/23830) to learn how to complete the self assessment, submit your findings to ISMP anonymously, promote interdisciplinary staff engagement to complete the assessment, and use the assessment reports to make perioperative medication safety improvements in their organization. Visit our perioperative assessment webpage (www.ismp.org/node/18027) to download a workbook with instructions, an Excel file to use to conduct the assessment, and to access the online assessment.

SAFETY briefs

Improved safety needed for pediatric pegfilgrastim use. ISMP has received error reports involving pediatric patients who are receiving injectable medications as outpatients and require the removal of "partial doses" from a prefilled syringe. For example, Amgen's **NEULASTA** (pegfilgrastim), which is used primarily for the prevention of chemotherapy-induced neutropenia, is only available in a 6 mg prefilled syringe, the intended dose for adults. Since Amgen is the product's sponsor, the same is true for biosimilar versions, **FULPHILA** (pegfilgrastim-jmdb), **UDENYCA** (pegfilgrastim-cbqv), **ZIEXTENZO** (pegfilgrastim-bmez) (**Figure 1**), and **NYVEPRIA** (pegfilgrastim-apgf). Yet the package insert includes a table for dosing pediatric patients under 45 kg that includes volumes less than 0.6 mL (6 mg). Furthermore, despite the weight-based pediatric dosing, confoundedly, the product labeling also states, "Note: The Neulasta prefilled syringe is not designed to allow for direct administration of doses less than 0.6 mL

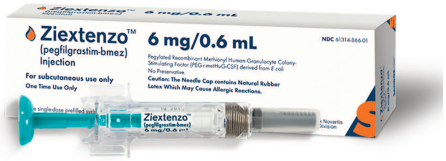

Figure 1. Pegfilgrastim-bmez (6 mg/0.6 mL) biosimilar syringe has no graduated markings.

(6 mg). The syringe does not bear graduation marks, which are necessary to accurately measure doses of Neulasta less than 0.6 mL (6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of less than 0.6 mL (6 mg) is not recommended due to the potential for dosing errors."

The error reports we have seen indicate that parents are sometimes instructed to withdraw a partial dose from the prefilled syringe using an empty sterile syringe and needle. While this is certainly not a risk-free option, parents of children who need this

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Screening for DPD Deficiency in Other Countries

Recently, the European Medicines Agency (EMA), the French regulatory agency (L'Agence nationale de sécurité du médicament et des produits de santé [ANSM]), and the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom, have all provided guidelines for preemptive DPD testing for patients scheduled for treatment with fluoropyrimidine chemotherapy.[3] But in the US, the National Comprehensive Cancer Network (NCCN) has not recommended universal pretreatment DPD deficiency screening,[4] and it is not currently the standard of care despite the known risks. Patient advocates have filed citizen petitions with the US Food and Drug Administration (FDA)[5] requesting a Boxed Warning in product labeling to reflect the need for patient screening. FDA-approved labeling for fluorouracil and capecitabine discusses DPD deficiency and the risk to patients, noting that patients with partial DPD activity may have increased risk of severe, life-threatening, or fatal adverse reactions caused by fluorouracil. So far, nothing in US product labeling recommends (or requires) screening patients for DPD deficiency prior to initiating fluoropyrimidine chemotherapy.

Pros and Cons of Screening for DPD Deficiency

If the technology exists to detect the deficiency through genotyping, and the consequences of not doing so in advance of therapy with a fluoropyrimidine drug potentially may lead to patient harm and death, why wouldn't providers preemptively screen patients? Several concerns have been raised regarding universal pretreatment screening.

Cost of screening. Insurance companies may not cover the cost of DPD genetic testing, citing the test to be investigational.[6] However, analyses of cost effectiveness show that screening prior to therapy, combined with preemptive dose reductions, is a cost-effective option compared to no screening, given the severe toxicity-related hospitalization of patients who have a DPD deficiency and receive full-dose fluorouracil or capecitabine.[7,8]

Potential delay in care. Providers have expressed concern that preemptive screening for all patients scheduled to receive fluoropyrimidine chemotherapy may cause a delay in treatment.[6] However, based on other discussions, it appears that the genetic testing can be completed in a reasonable amount of time. According to laboratory personnel who we spoke with, in-house testing results can be available in 2 to 3 days, and external laboratory testing results can be available in 3 to 10 days. In most (but not all) cases, waiting for the genetic testing results is reasonable as workup and decisions are being made regarding cancer treatment. Or, at least screening can take place concurrently with therapy initiation since coordinating the start of therapy may take a few days.

Potential lack of consensus on dosing. Some clinicians have also cited a lack of consensus on preemptive dose reductions for DPD deficiency to be a barrier to widespread testing. However, clear guidance is available from the Clinical Pharmacogenetics Implementation Consortium (CPIC), a leading authority on implementing pharmacogenetic testing for patient care.[2,3] Their dosing recommendations address the varying degrees of DPD deficiency for safe and effective use of fluoropyrimidines in all patients.[2]

Potential decreased efficacy against cancer. Another concern raised is the uncertainty and potential negative impact on treatment efficacy if preemptive testing leads to a dose reduction. However, pharmacokinetic studies show that patients with DPD deficiency have significantly increased exposure to fluoropyrimidines.[8] It has also been found that overall survival and progression-free survival of DPD-deficient patients who preemptively receives a dose reduction were not negatively impacted.[9]

NCCN does not support routine screening. The *NCCN Clinical Practice Guidelines in Oncology for Colon Cancer* acknowledge evidence from published studies that support the feasibility, cost effectiveness, and improved safety of pretreatment DPD deficiency

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drug may have no other choice since pegfilgrastim injection is not available in a vial. If used in a hospital, pharmacists would be unlikely to dispense the prefilled syringe for administration when only a partial dose is prescribed. Instead, the exact dose would be prepared under a laminar flow hood. That being said, this is a significant safety issue for many outpatient pediatric patients receiving the drug, especially since not all pharmacists are aware of the issue.

One hospital-based specialty and retail pharmacy told us they typically provide parents/patients with an empty sterile vial and a sterile syringe and needle. They instruct parents/patients to inject the entire contents of the prefilled pegfilgrastim syringe into the empty vial, withdraw the prescribed dose using the sterile syringe and needle, and discard the medication remaining in the vial. They have built standard instructions in the pharmacy computer system, and staff are now creating a standard teach-back process to confirm the parent's/patient's understanding and ability to withdraw the prescribed dose from the vial.

This is not ideal, and for ongoing use in ambulatory care, some specialty/retail pharmacies may feel they have no choice but to dispense full syringes of the drug and have parents measure out the correct partial dose. In some cases, parents have accidentally given their child the full 6 mg dose. In one reported case, a 40 kg patient was prescribed Udenyca 4 mg, but because the syringe is not graduated, the patient/family was unable to measure the dose. The prescriber eventually told the patient/family to administer the full 6 mg. The hospital that reported this event has added flags in their pharmacy system to promote counseling during outpatient dispensing, but this may not be a feasible strategy in other non-hospital-based community pharmacies.

ISMP has contacted the US Food and Drug Administration (FDA) about this concern. Amgen and biosimilar manufacturers need to provide a vial presentation and/or add graduation marks to prefilled syringes so smaller doses can be measured. Also, in conjunction with making a vial available, syringe manufacturers will need to make pediatric syringes available to deliver smaller doses.

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screening.[4,8,10] In the US, *DPYD* genotyping is the main test used to determine a DPD deficiency, which is defined as the presence of one or more variant *DPYD* alleles that are known to result in a DPD protein with partial or complete loss of function. However, the NCCN Colon Cancer Panel concludes that "because fluoropyrimidines are a pillar of therapy in [colorectal cancer] and it is not known with certainty that given *DPYD* variants are necessarily associated with this risk, universal pretreatment *DPYD* genotyping remains controversial and the NCCN Panel does not support it at this time."[4]

Other. It should also be mentioned that uridine triacetate (**VISTOGARD**) has been used to treat patients with pyrimidine toxicity due to DPD deficiency, even when given past 96 hours as recommended in the product labeling.[11] Such use, however, is not included in FDA-approved product labeling.

Conclusion

In reviewing the literature surrounding the hesitancy to adopt universal DPD deficiency screening prior to the use of fluoropyrimidines, the risk of patient harm and potential fatality seems clear when administering fluoropyrimidines to patients with a DPD deficiency, while the hurdles to implement widespread testing seem to be manageable. So, ISMP joins others who ask the question, "Why not?"

References

1) Wigle TJ, Tsvetkova EV, Welch SA, Kim RB. DPYD and fluorouracil-based chemotherapy: mini review and case report. *Pharmaceutics*. 2019;11(5):199.
2) Amstutz U, Henricks LM, Offer SM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing: 2017 update. *Clin Pharmacol Ther*. 2018;103(2):210-6.
3) Ciccolini J, Milano G, Guchelaar HJ. Detecting DPD deficiency: when perfect is the enemy of good. *Cancer Chemother Pharmacol*. 2021;87(5):717-9.
4) Benson AB, Venook AP, Al-Hawary MM, et al. Colon cancer, version 2.2021, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2021;19(3):329-59.
5) Surprenant KE (citizen's petition). Regulations.gov. Posted November 18, 2020. Accessed June 10, 2021. www.ismp.org/ext/725
6) Lau-Min KS, Varughese LA, Nelson MN, et al. Clinician perspectives on preemptive pharmacogenetic testing to guide chemotherapy dosing in patients with gastrointestinal malignancies. *J Clin Oncol*. 2021;39(3)(suppl):54.
7) Brooks GA, Tapp S, Daly AT, Busam J, Tosteson ANA. Cost effectiveness of DPYD genotyping to screen for dihydropyrimidine dehydrogenase (DPD) deficiency prior to adjuvant chemotherapy for colon cancer. *J Clin Oncol*. 2021;39(3)(suppl):55.
8) Deenen MJ, Meulendijks D, Cats A, et al. Upfront genotyping of DPYD*2A to individualize fluoropyrimidine therapy: a safety and cost analysis. *J Clin Oncol*. 2016;34(3):227-34.
9) Henricks LM, van Merendonk LN, Meulendijks D, et al. Effectiveness and safety of reduced-dose fluoropyrimidine therapy in patients carrying the DPYD*2A variant: a matched pair analysis. *Int J Cancer*. 2019;144(9):2347-54.
10) Henricks LM, Lunenburg CATC, de Man FM, et al. DPYD genotype-guided dose individualisation of fluoropyrimidine therapy in patients with cancer: a prospective safety analysis. *Lancet Oncol*. 2018;19(11):1459-67.
11) Ma WW, Saif MW, El-Rayes BF, et al. Emergency use of uridine triacetate for the prevention and treatment of life-threatening 5-fluorouracil and capecitabine toxicity. *Cancer*. 2017;123(2):345–56.

Patient administration errors with the use of alprostadil urethral inserts

Patients have incorrectly used the product **MUSE** (acronym for medicated urethral suppository for erection), a urethral alprostadil suppository prescribed for erectile dysfunction. The medication is available preloaded into an applicator system (**Figure 1**) and is administered by inserting the stem into the urethra after urination (to ensure the urethra is wet) and pressing the applicator button. Each applicator system is wrapped in a foil pouch. Six applicator systems are packaged in a carton. Patients have reported confusion regarding how to properly use this product, resulting in ineffective medication and sometimes leading to urethral hemorrhage.

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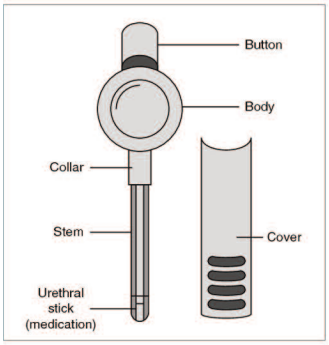

Figure 1. Muse applicator system.

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Drug manufacturers need to stop printing barcodes across round surfaces! A hospital discovered a billing issue with its rabies immune globulin (human) 2 mL vial, **KEDRAB** (manufactured by Kamada, distributed by Kedrion Biopharma), while auditing their 340B program. They were not receiving the product at the correct 340B contract price because they had "no documented administrations" of it at the hospital. However, the hospital had frequently been reordering the product, so it clearly was being used. The pharmacy researched the problem and found numerous instances of not billing for the medication. The 340B program software links the billing of the doses administered to how much is being used. It turned out that the medication was not being charted on the medication administration record (MAR). Despite nurses thinking the product label scanned, documentation failed because the barcode on the product is printed on the label horizontally on the curve of the round vial (**Figure 1**), so it could not be completely read by the laser scanner.

Figure 1. Edges of the Kedrab barcode are not captured by a barcode scanner.

This situation obviously creates a financial issue but also a patient safety issue since the medication is not being scanned for verification. The issue is also problematic because the dose may be repeated if another practitioner thought it had not been administered, or since the healthcare team might make incorrect decisions about patient care based on an inaccurate medication administration history.

The vial is packaged in a carton that has a scannable barcode, but nurses usually discard this after removing the vial, so it is no longer available at the bedside during administration. While not ideal, for now, this pharmacy is asking nurses to hold on to the carton to scan its barcode at the bedside before administering the product, rather than scanning the barcode on the vial. At a minimum, nurses should manually document administration on the MAR if the carton has already been discarded. The pharmacy will be reviewing reports daily to verify that the

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One factor contributing to these errors has been the lack of adequate verbal patient education. Patients have reported that neither the prescriber nor the dispensing pharmacist have explained how to administer the medication. In one case, the patient used the product with the protective cover still in place. Another factor for confusion has been a breakdown in providing written instructions for use. Despite the professional package insert stating that "a Patient Package Insert (PPI) must be given to each patient at the initiation of therapy," patients are not always given one. This gap can be attributed to several issues. First, the manufacturer's information intended for patients, including step-by-step patient instructions for administration, is printed at the end of the professional package insert meant for healthcare professionals. Both pharmacists and patients could easily miss these essential patient instructions, and pharmacists may not give the patient what appears to be a professional package insert. Also, this information is confusingly referred to as "Patient Information" and not a "Patient Package Insert" as stated in the professional package insert." Nevertheless, pharmacists rarely hand patients a professional package insert, although this could be substituted for a PPI. Still, it would be far better if at least two documents labeled as a "Patient Package Insert" were in each carton.

For patients who do not receive the patient information, there are instructions on the back of each foil pouch that direct patients to two external manufacturer resources for information—the product-specific website (www.muserx.net) and a phone number to the company's medical information center. However, during the past 3 weeks, this website did not appear to be working, and the phone number did not lead to a direct line that walks patients through the administration process. In fact, we were unable to locate a functioning website or phone number for the manufacturer listed in the product labeling, Meda Pharmaceuticals of Somerset, NJ. The website needs to be made accessible as soon as possible, with separate updated instructions identified as a PPI. Also, direct telephone access needs to be available for patients who need their questions answered.

It is critical for prescribers and dispensing pharmacists to familiarize themselves with the administration process for Muse. They must teach patients receiving Muse how to administer the medication safely and verbally verify the patient's understanding. They also must make sure to provide the patient with the manufacturer's professional package insert with the included patient information, if one is available. Other than diagrams in the product labeling, the manufacturer does not appear to provide additional information to help patients properly use Muse. There are, however, several useful videos about Muse on YouTube, including this one: www.ismp.org/ext/723. But the instructions may be challenging to find on YouTube because there are other products and a music artist using the name "Muse." It helps to include something else about the product in the search, such as "Muse suppository" or "Muse alprostadil."

ISMP has interacted with the US Food and Drug Administration (FDA) regarding this product and the issues with the patient instructions. It should be mentioned that there are other medications and dosage forms packaged in cartons containing multiple units that may not be accompanied by an adequate number of PPIs if the carton is split for prescription quantities less than a full carton. For products that are routinely dispensed in quantities less than a full carton (including Muse), manufacturers should consider including additional patient instructions for each individual drug product that might be dispensed. FDA should take this into account when interacting with manufacturers.

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medication was charted as given, as well as billed appropriately.

ISMP has repeatedly mentioned this problem in the past with barcodes on the labels of round ampules, vials, inhaler canisters, and oral liquid bottles, including most recently in our January 16, 2020, issue (fentaNYL ampule from Hospira), in our March 11, 2021, issue (cisatracurium vial from AbbVie), and in our June 17, 2021, issue (sodium polystyrene sulfonate suspension from CMP Pharma). Linear barcodes on round ampules, vials, inhaler canisters, and oral liquid bottles should only be printed perpendicular to the curve of the container, usually along the edge of the label on one side, rather than horizontally around the curve of the container. Purchasers should avoid products with curved barcodes, when possible, if scanning technology is used during product selection and administration. The US Food and Drug Administration (FDA) should consider publishing an informative media release about this problem that is directed at drug manufacturers. The problem should also be addressed in the finalized FDA draft Guidance, *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors*.

Special Announcements

Please take our survey!

We have extended the deadline to **July 30, 2021**, for taking the ***ISMP Survey on the 2020-2021 Targeted Medication Safety Best Practices for Hospitals***. Survey statistics tell us it will take about 15 minutes to complete by visiting: www.ismp.org/ext/702.

Free ISMP webinar

Join us on **July 20, 2021**, for a **FREE** webinar on ***The Inside Track on Drug Naming Safety Standards***. Hear from our panel of experts about the benefits of drug name testing. To learn more, visit: www.ismp.org/node/25216.

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ISMP Medication Safety Alert!® ActionAgenda

One of the most important ways to prevent medication errors is to learn about problems that have occurred in other organizations and to use that information to prevent similar problems at your practice site. To promote such a process, the following selected items from the April – June 2021 issues of the ***ISMP Medication Safety Alert! Acute Care*** have been prepared for leadership to use with an interdisciplinary committee or with frontline staff to stimulate discussion and 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 number to locate additional information. Look for our high-alert medication icon under the issue number if the agenda item involves one or more medications on the ***ISMP List of High-Alert Medications*** (www.ismp.org/node/103). The Action Agenda is also available for download in a Microsoft Word and Excel format (www.ismp.org/node/25693) that allows expansion of the columns in the table designated for organizational documentation of an assessment, actions required, and assignments for each agenda item. Continuing education (CE) credit is available for nurses at: www.ismp.org/nursing-ce.

Key: ⚠ — ISMP high-alert medication

Issue No.	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Concentrated potassium chloride given via intravenous (IV) push during a cardiac arrest (code) causes death					
(11, 12) ⚠	A patient died during a code due to the administration of concentrated potassium chloride via IV push. Four root causes were identified: 1) inadequate number of caregivers present during the code because it was not announced hospital-wide; 2) lack of communication and incorrect assumptions among the code team; 3) pharmacy dispensed a vial of concentrated potassium chloride without question; 4) a gap in supervision led a nurse fellow to practice beyond the scope of his training. Also, when reviewing this event with ISMP staff, a senior pharmacy student thought IV administration of undiluted potassium chloride would only cause vein sclerosis.	Announce all codes hospital-wide or via a code beeper system to ensure adequate team members are present. Specify the route and method of drug administration and communicate the reason for medications rarely used during a code. Repeat all medication orders and evaluate communication post-code. Nurse fellows and other learners should participate in codes only after advanced cardiac life support (ACLS) training. Also, preceptors should reinforce potassium chloride safety and teach students that undiluted IV administration is deadly.			
Additional strategies to improve complete delivery of small-volume intermittent infusions					
(7)	Small-volume intermittent intravenous (IV) infusions administered using a primary administration set may lead to underdosing due to the residual volume left in the tubing. If the same tubing is used later for medication or fluid administration, the residual volume in the tubing could result in an inadvertent bolus of the medication or a drug incompatibility.	Create reminders to administer small-volume infusions using a secondary set. Add an appropriate carrier fluid to order sets to flush the residual drug from the tubing after the intermittent infusion has been administered. List an accurate volume to be infused (VTBI), including the manufacturer's overfill, volume of each additive, and the bag volume, on the pharmacy label for use when programming the pump. Set pump alarms to detect unopened clamps (if capable).			

Issue No.	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Error trends with the emergency use authorization (EUA) coronavirus disease 2019 (COVID-19) vaccines					
(8)	Since COVID-19 vaccine administration began, errors have been reported which can be categorized as general errors (e.g., wrong dose, wrong age, wrong injection technique); errors with the two-dose mRNA vaccines (e.g., wrong vaccine for the second dose, wrong interval); dilution errors (Pfizer-BioNTech vaccine); and giving patients a two-dose reminder on the Vaccination Record Card after a single-dose Janssen vaccine has been administered.	Establish a scheduling system that does not allow patients younger than the authorized ages per vaccine to schedule an appointment. Confirm the date of the first mRNA vaccine dose and manufacturer before administering a second dose. When possible, have pharmacy prepare and label vaccine doses. On the Vaccination Record Card for patients receiving the single-dose Janssen vaccine, cover references to a second dose with a note that only a single dose is needed.			
Careful identification of US Food and Drug Administration (FDA)-approved color additives is required for patients with allergies					
(12)	Ibuprofen oral suspension was prescribed for a child with a red dye allergy. The principal display panel on the ibuprofen bottle (Perrigo, prescription-only size) listed a yellow #6 additive. The pharmacist and technician believed this to be the only color additive but later found that red #33 was listed in the package insert (PI). According to federal regulations, oral prescription drugs are not required to list all inactive ingredients on the container label, outside wrapper, or in the PI (although most list these voluntarily in the PI).	If patients have a known food dye intolerance or allergy, list it in a standardized, visible location on all drug-related pages or electronic health record screens. Read the PI or *Drug Facts* label, and if you are not sure whether a medication contains a color additive, call the manufacturer. If a patient cannot take a medication critical to their recovery or health due to the color additive in the medication, compounding pharmacies might be able to provide the medication without the allergen.			
Maximizing automated dispensing cabinet (ADC) medication removal and restocking accuracy					
(10)	In the pharmacy, scanning only one item when multiple items of the same product need to be restocked in an ADC can lead to errors, especially with drugs that have look-alike names/labeling/packaging. ADC stocking errors may also occur if nurses are permitted to return intact medications to an ADC drawer/bin, particularly without scanning the medication's barcode.	To maximize the accuracy of ADC stock, use strips of tablets and unopened cartons, or rubber band the same products together before a pharmacist's verification, which should include a visual inspection and barcode scanning of all products to verify the ADC restock before distribution. Allow nurses to return intact medications to an ADC locked-lidded pocket only if barcode scanning is utilized. Otherwise, use a one-way ADC bin for pharmacy restocking.			

Issue No.	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Administering patient-controlled analgesia (PCA) to patients during magnetic resonance imaging (MRI)					
(12) ⚠	For an MRI patient who was receiving both morphine PCA and a plain fluid maintenance infusion, several feet of extension tubing was added to the PCA tubing so the pump could be left outside the room. The patient decompensated shortly after starting the MRI, and it was discovered that the patient had received a bolus of morphine (56 mg) from the long extension tubing when the patient's maintenance infusion was initiated at an undisclosed rate. Another patient receiving **HYDRO**morphone PCA experienced a similar event. Both patients required treatment with naloxone.	Establish a process to address pain control of MRI patients receiving PCA. This requires training staff, using MRI-compatible PCA pumps, providing alternative pain management therapy, and/or determining where to connect the extension sets and PCA line if the patient has a primary infusion and/or needs bolus doses of contrast media. Also, develop guidelines for monitoring MRI patients who are receiving an intravenous (IV) opioid. Many of the risks posed by PCA also pose safety concerns with other drug infusions (e.g., anticoagulant, insulin, vasopressor) that must be maintained during an MRI.			
Heparin flushes should be scanned					
(7) ⚠	Heparin flush syringes (Medefil) come in 1 unit, 10 units, and 100 units per mL concentrations, each in a different color syringe. However, each concentration comes in various fill volumes using the same color, which makes the syringes look similar. Nurses may not be required to scan heparin (or saline) flushes, increasing the risk of a mix-up reaching a patient.	Require barcode scanning of heparin (and saline) flushes to help identify possible mix-ups between the different volumes and concentrations of heparin syringes as well as other medications or flush solutions prepared in similar-looking syringes.			
Patients received EPINEPHrine instead of the Moderna coronavirus disease 2019 (COVID-19) vaccine					
(7) ⚠	A nurse mistakenly administered pharmacy-prepared syringes containing **EPINEPH**rine to two patients instead of pharmacy-prepared syringes of the COVID-19 vaccine. The pharmacy had prepared batches of syringes containing **EPINEPH**rine and COVID-19 vaccines and dispensed them in separate plastic bags, but the pharmacy-prepared syringes looked very similar.	COVID-19 vaccination sites should stock **EPINEPH**rine autoinjectors rather than pharmacy-prepared syringes, so the vaccine and **EPINEPH**rine syringes look different. The **EPINEPH**rine autoinjectors and vaccine syringes should be kept in different storage locations but close enough to be quickly retrieved. Consider storing the **EPINEPH**rine autoinjectors in an anaphylaxis kit at the vaccination site.			

Issue No.	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
ADRENALIN (EPINEPHrine) vials (Par Pharmaceutical) look like Pfizer-BioNTech coronavirus disease 2019 (COVID-19) vaccine vials					
(11) ⚠	Adrenalin vials look similar to COVID-19 vaccine vials as they are the same size and shape with purple caps and mostly black print on white labels. Both of these vials may be found at COVID-19 vaccination sites, and they could be mixed up due to their visual similarities.	Avoid storing these medications near each other. If possible, use barcode technology to scan Adrenalin vials prior to administration. Use **EPINEPH**rine autoinjectors instead of vials since they look visually different from the COVID-19 vaccine vials.			
Liquid medication administered via cecostomy instead of gastrostomy tube (G-tube)					
(10)	A child was inadvertently given liquid acetaminophen, lansoprazole, and sucralfate through a cecostomy button extension set because it looked similar to the extension set typically used with a G-tube button. Medications administered via a cecostomy are not absorbed well in the large intestine.	Pharmacy should provide liquid enteral medications in ENFit syringes, which could then be used with ENFit extension sets that are only used for the G-tube. Legacy extension tubing should be used for the cecostomy since it is not compatible with ENFit syringes and would prevent this type of error.			
Preferred vs. legal name of transgender patients in automated dispensing cabinets (ADCs)					
(11)	A transgender patient was known by a preferred name. When this patient had a sudden cardiac arrest, the team could not find the patient by their preferred name in the ADC because only their legal name was displayed. Electronic health records (EHRs) include fields for patients' preferred names, but ADCs only receive the legal name from the EHR.	Vendors should consider updating ADC technology to allow the preferred name to transfer from the EHR. On medication labels, the legal name and preferred name should both be documented accordingly. Healthcare providers should recognize the potential for name confusion during patient care.			
Dr. Reddy's glass naloxone syringes are not compatible with Clave/MicroClave (ICU Medical) connectors					
(7)	A Dr. Reddy's prefilled glass naloxone syringe was attached to a patient's intravenous (IV) MicroClave needlefree connector, but depressing the plunger to administer the medication was next to impossible. The glass syringe tip causes the pin in the MicroClave access to break off and become lodged within the syringe nozzle, preventing the flow of medication.	Purchase other naloxone products that are compatible with Clave/MicroClave needless connectors. If Dr. Reddy's syringes are your only option, administer the naloxone intramuscularly or via the nasal route using an atomizer, not by the IV route.			