

Nurse AdviseERR®

Educating the Healthcare Community About Safe Medication Practices

Two unsafe practices:

Administration of a product with a precipitate and reuse of a saline flush syringe

Two events recently brought to our attention have again thrust unsafe injection and infusion practices into the limelight. One involves the dispensing and intravenous (IV) administration of a pharmacy-prepared product despite a visible precipitate, and the other involves the reuse of prefilled saline flush syringes for multiple patients, leading to the transmission of bloodborne diseases. We have not previously published the scattered reports we received related to these unsafe practices, initially believing they were isolated cases. However, these recent events brought to our attention that this may be a more widespread problem, which healthcare providers should address with clinical training programs and improved monitoring to ensure adherence with safe practices.

Dispensing and administering a product with a visible precipitate

To ensure the safe intravascular delivery of medications and solutions, practitioners must be observant for potentially dangerous precipitates (**Figure 1**) often caused by drug or diluent incompatibilities (e.g., acid-base reactions, mixing oppositely charged organic drug ions).¹

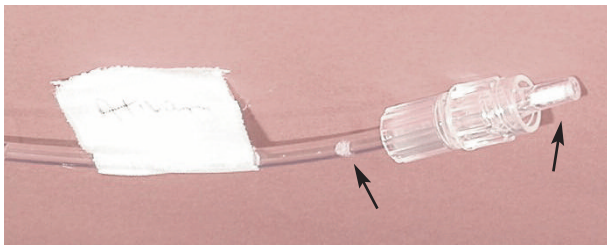


Figure 1. Example of precipitate (LORazepam) in IV tubing.

In an analysis of more than 300 drug incompatibilities reported to the Pennsylvania Patient Safety Authority between 2009 and 2016, almost one in five mentioned the formation of a precipitate.² Precipitation reactions are usually rapid and can be observed as crystals, haziness, or turbidity. If a precipitate is observed, the drug or solution should not be administered. The precipitate can lead to drug inactivation and subsequent therapeutic failures, catheter occlusions, and varying levels of harm due to particulate embolization, ranging from thrombophlebitis to multi-organ failure or even death.³ The consequences can be particularly severe in pediatric patients.⁴

Since 1998, a total of 23 cases of precipitation have been reported to the ISMP National Medication Errors Reporting Program (ISMP MERP). In 17 cases, a pharmacist or nurse (or patient/caregiver in the home setting) noticed the precipitate and immediately remedied the problem or stopped the injection or infusion. Some of these cases involved compounding or flushing errors in which the wrong diluent, flush or base solution, or concentration/dose was used, which resulted in the formation of a precipitate. However, in 4 cases, the medication or solution was administered despite observing the precipitate.

In one of these cases, a patient with no previous cardiac or pulmonary disease died. A bag of calcium gluconate and potassium phosphate mixed in saline in the pharmacy appeared cloudy prior to administration, but the nurse still started the in-

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SAFETY wires



Don't dilute ProveyBlue in normal saline.

Due to the current drug shortage of methylene blue, a hospital switched from the generic product it normally used to the brand product **PROVAYBLUE**, which the US Food and Drug Administration (FDA) approved last year. This drug was prescribed for a patient with encephalopathy from ifosfamide (www.ismp.org/sc?id=2895). The pharmacist who built the electronic order set for ProveyBlue in the computer system noticed that, in Lexicomp, under the preparation for administration section for methylene blue, it states: "For the treatment of ifosfamide-induced encephalopathy treatment (off-label use), case reports cite administering the dose undiluted, diluted in 50 mL NS or D5W, or diluted in 250 mL of D5W." The hospital's previous order set for methylene blue listed 0.9% sodium chloride injection as the diluent, so no change was made for ProveyBlue. However, the pharmacist missed additional information in the same section of the Lexicomp methylene blue monograph that was more specific to ProveyBlue. It states: "Dilution not required. In order to avoid local pain (especially in pediatric patients), may be diluted in 50 mL of D5W. Do not dilute in NS (the solubility of methylene blue is reduced)."

Because the order set for ProveyBlue was built incorrectly, ProveyBlue was compounded using a base solution of 0.9% sodium chloride. This was dispensed, and once administration began, a precipitate formed in the intravenous (IV) tubing. Because the nurse did not report the precipitation during the first round of therapy (it may not have been readily visible because of the dark blue color of the product), the error was not immediately identified. Later, another nurse reported the precipitate to the pharmacy when a new bag was started for the same patient, at which time the dilution discrepancy between the methylene

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fusion. About an hour later, the patient was found in respiratory distress which quickly progressed to a fatal cardiac arrest. A different nurse had previously abandoned an attempt to administer the same solution due to its cloudy appearance, although she had not yet contacted the pharmacy. The nurse who then administered the solution decided to hang it after referencing a flawed hospital protocol that stated products with precipitates could be infused under “close observation” due to the risk of “sudden death.” An autopsy showed scattered pulmonary emboli, and the death was determined to be accidental and related to the infusion of the precipitated electrolyte infusion.

In the ISMP MERP database, there were two additional events in which nurses attempted to administer solutions despite observed precipitates. But fortunately, rapid IV line occlusions led to their discontinuation, although in one case, the solution was reinfused into another vein until that line also became occluded.

In 2015, ISMP learned of another event in which an 11-month-old baby received daily etoposide infusions over a 5-day period despite the presence of visible precipitates within the solution. The baby had a rare form of cancer, and four oncologists had worked together to create a custom chemotherapy treatment plan. Unfortunately, the dose of etoposide was mistranscribed as 33 mg per kg per day, instead of the correct dose of 3.3 mg per kg per day, for 5 days. The high concentration of the etoposide, which was diluted in 100 mL of normal saline, caused the drug to precipitate. Despite frequent occlusions and the need to constantly flush and reaccess the IV access port, none of the nurses reported the precipitate to a pharmacist or oncologist or stopped the infusion. Had they done so, perhaps the 10-fold dosing error could have been detected before the 5 days of therapy had been administered. When we learned of the error, the baby was being closely monitored for possible liver, renal, bone marrow, neurologic, and respiratory damage secondary to etoposide toxicity and particulate administration.

ISMP recently received another report about a compounding error with **PROVAYBLUE** (methylene blue) that led to precipitation of the drug and IV administration despite potentially visible particulates in the solution or IV tubing (see the **SAFETY wire** starting in the right column on page 1).

Reuse of prefilled saline flush syringes

According to the Centers for Disease Control and Prevention (CDC), unsafe injection practices have affected more than 150,000 patients since 2001, including more than 50 documented outbreaks of viral hepatitis or bacterial infections.⁵ While many practitioners follow the CDC safe injection practices guideline,⁶ a survey of more than 5,000 practitioners about the use of needles, syringes, and vials suggests that some may be placing patients at risk for transmission of bloodborne diseases.⁷ For example, 1% of the survey respondents admitted to sometimes or always reusing a syringe for more than one patient.

We first learned about the unsafe practice of reusing a prefilled saline flush syringe from a 2013 press release issued by a New York hospital that was investigating possible disease transmission in 236 patients hospitalized during a 3-month period.⁸ In that case, a single nurse had been reusing prefilled saline syringes to flush the IV lines of multiple patients, mistakenly believing that the practice was safe. Luckily, no cases of disease transmission had been identified at the time of the press release.

More recently, the March 10, 2017, issue of *Morbidity and Mortality Weekly Report (MMWR)* described a very similar event, this time in a Texas hospital. A nurse who worked in a telemetry unit had been reusing prefilled saline syringes to flush the lines of multiple patients, which led to a case of hepatitis C transmission.⁹ The

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blue products was discovered. Fortunately, the patient was not harmed and the error was caught before any additional patients received the incorrectly compounded product. Strangely, it may not be that uncommon for IV infusions to continue even if a precipitate is noticed, without reporting the event to the pharmacy. For more on this topic, please see the feature article.

**Tresiba U-200 won't allow odd number dosing of insulin units.**

With the introduction of the **TRESIBA** (insulin degludec) U-200 pens comes a chance for dosing errors. A pharmacist recently reported that a physician prescribed 25 units daily of Tresiba U-200. This product is only available in the Novo Nordisk FlexTouch insulin pen. An odd numbered dose is not possible with U-200 because the pen only allows dosing increments in even numbers, starting at 2 units and going up to 160 units. In this case, an elderly patient tried to dial 25 units by estimating the proper position between 24 units (marked on the pen) and a notch or score that represents 26 units (**Figure 1**). Due to the design of the pen, the insulin will not be administered unless the pen is correctly set to a dose—24 or 26 units in this case.



Figure 1. Tresiba U-200 pen allows dosing increments of 2 units, so only even numbered doses can be delivered.

It's important for healthcare professionals to be aware of the difference between U-100 pens and the U-200 Tresiba pen. Although the U-200 pen WILL allow doses from 2 to 160 units (in even numbers only, 2 units at a time), prescribers should consider providing a U-100 pen when smaller or odd numbered doses must be administered, reserving U-200 pens for patients requiring larger, even numbered doses.

**Why color-coding injectables by drug class can be dangerous.**

A hospital recently converted from ePHEDrine ampuls to vials from Éclat Pharmaceuticals. Since then, there have been several instances at the hospital where the drug vial was

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unsafe practice was discovered after noticing that the nurse would often leave a partially filled saline flush syringe near a computer work station. When a nurse manager investigated this practice, the nurse voluntarily reported reusing syringes during the previous 6 months, believing it was cost-effective and safe if no fluids had been withdrawn into the syringe prior to injecting the saline. The nurse had been working on the unit for 18 months but had not been taught that this was an unsafe practice.

Because all telemetry unit patients were required to have IV access, all 392 living patients potentially exposed to this unsafe practice were notified about the possible exposure to bloodborne diseases and the need for laboratory testing. One of two patients who tested positive for hepatitis C had been admitted to the unit during the same time as a patient with known preexisting chronic hepatitis C infection. Genotyping and molecular sequencing identified that both were infected with an identical strain, which accounts for only about 1% of all hepatitis C infections in the US. The CDC concluded that at least one of the hepatitis C infections was likely transmitted as a result of inappropriate reuse and sharing of the saline flushes between multiple patients.⁹

ISMP is concerned that the reports of IV drug administration despite observed particulates, and the reuse of prefilled saline flush syringes, are signals of more widespread unsafe practices that illustrate the need for ongoing education and improved monitoring. Given the potential for harm associated with these unsafe practices, several opportunities exist to reduce the risk of errors.

Education

Provide initial orientation and annual education on injection and infusion safety, and include new and temporary nurses. Assess and reinforce practitioner competence associated with even the most basic concepts of infection control and aseptic technique, including recognition that any form of syringe and/or needle reuse is dangerous and should be prohibited. All nurses, pharmacists, and pharmacy technicians should also be taught to observe medications and solutions for precipitates, and to avoid dispensing or administering an injection or infusion if precipitates are visible or a solution that should be clear is cloudy. Provide actual examples or pictures of drugs that have precipitated¹⁰ so practitioners who have never seen this reaction know exactly what to look for.

Also, be sure practitioners understand how to identify and avoid drug incompatibilities when preparing and administering medications or solutions or flushing IV lines (e.g., thoroughly flushing the line before administering an incompatible drug, administering certain medications through a separate injection port or site). The use of an in-line filter for solutions that are prone to precipitation can also help prevent particulates from entering the body; however, precipitates can still form in the tubing below the filter, and filters may become blocked, signaling a need to investigate.²

Policies and procedures

Review organizational policies and procedures related to safe injection and infusion practices to ensure that the principles of infection control, aseptic technique, the CDC safe injection practices guideline,⁶ and the ISMP Safe Practice Guidelines for Adult IV Push Medications¹¹ have been incorporated. Policies and protocols should also be very clear regarding the need to avoid or immediately discontinue any injection or infusion if particulates are observed in medications or solutions.

Surveillance

It is essential to monitor adherence with proper injection and infusion techniques in
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mistaken as **EPINEPH**rine, manufactured by PAR Pharmaceutical. Both products are available in small vials with purple caps, as noted by the person who sent us the report. Purple is also on the vial labels, and the generic names of the drugs can look similar, especially with the narrow print used by Éclat on its **ePHED**rine label (**Figure 1**). Also, these drugs are often stored near each other in areas such as labor and delivery and the operating room.



Figure 1. Although somewhat different in overall appearance, the purple cap and label may have contributed to several mix-ups.

What's important to know is that this report represents our first notification about a medication error where drug class color-coding may have played a role, at least indirectly. Purple is the standard color for *user-applied* labels on syringes of vasopressors in the operating room (OR) (ASTM D4774-06 Standard Specification for User Applied Drug Labels in Anesthesiology). However, “user-applied” (in the control of individual anesthesiologists or anesthesiologists) does not mean the standard should be applied by manufacturers for commercial drug vials that contain vasopressors, which, whether by design or coincidence, seems to be the case here. Although both drugs are vasopressors, mix-ups between **ePHED**rine and **EPINEPH**rine are dangerous, as noted in our April 17, 2003 issue (www.ismp.org/sc?id=2864).

Many hospitals also purchase prefilled syringes from 503b compounding pharmacies that unnecessarily use the standard colors for user-applied labels. But what may be safe on syringes within the OR environment may not be safe in other areas of the hospital. With commercial vials, similarity
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all settings where medications are prepared and administered. Consider developing a checklist¹² based on the CDC safe injection practices guideline⁶ that can be used to conduct the surveillance process and collect the data. Syringe reuse, if identified, should be immediately corrected, and patients should always be notified of any potential exposures and the need for testing.⁹

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in appearance is enhanced by the use of similar colors across a drug class.

The ASTM color scheme is used for other drug classes such as opioids, neuromuscular blockers, beta blockers, and induction agents. It was never meant for commercial drug vials, especially high-alert drugs where individual agents within the class may have varying potencies and pharmacologic effects. We agree with the reporter's concern about the potential for mix-ups attributed to the purple caps. We hope that the US Food and Drug Administration (FDA), Éclat, PAR, and other manufacturers of commercial drug vials will stay away from any type of color-coding by drug class.



No, not methotrexate. Despite its name, **MTX TOPICAL PAIN** does not contain methotrexate or **mitoXANTRONE**, both cancer drugs associated with the dangerous abbreviation "MTX" which has led to mix-ups between them. When we saw "MTX" used for this over-the-counter (OTC) topical lidocaine 4% and menthol 1% patch sold by Unik Pharmaceuticals, we were taken aback. Perhaps more concerning is that arthritis sufferers are commonly treated with methotrexate and may be misled by the "MTX" on this patch. The image on the product's package also implies that it is used to treat joint pain, which it does not. Methotrexate is also used to treat psoriasis, a disease characterized by skin lesions, while the MTX Topical Pain product specifically warns against use in patients with damaged skin.

This combination of lidocaine and menthol ingredients is marketed under the OTC Drug Monograph process "for temporary relief of pain and itching associated with minor burns, cuts, scrapes, and minor skin irritations." OTC products in compliance with an OTC Drug Monograph may be marketed without submitting a product name for review or undergoing a preapproval review by the US Food and Drug Administration (FDA). According to FDA, the monographs establish conditions under which certain OTC active ingredients are "generally recognized as safe and effective." FDA has been alerted to this error-prone abbreviation. We would appreciate hearing from readers who may have experienced an issue with this OTC product.

New!

< ISMP International > Safe Medication Management Fellowship

ISMP is now accepting applications for
a unique **2-year International Fellowship**

Sponsored by: Baxter International

Location and Term: The 2-year International Fellowship, sponsored by Baxter International, begins on **September 1, 2017**, at the Horsham, Pennsylvania (near Philadelphia) office of the Institute for Safe Medication Practices (ISMP). Relocation to the Horsham/Philadelphia area is required.

Qualifications: The International Fellow must:

- Have an advanced degree in healthcare (e.g., PharmD, master's degree)
- Have at least 1 year of experience in a clinical role in an acute care setting
- Be fluent in written and spoken English
- Be a US citizen or have official documentation that allows him or her to remain in the US for 2 years and travel internationally for a week or more at a time

Description: The International Fellowship will help train a medication safety leader seeking a long-term career at an international level. The Fellow will be involved in global medication safety initiatives, address worldwide safety issues, and help increase global reporting of medication errors. They also will work directly with international professional organizations and medication safety centers, and attend multi-country medication safety meetings and events. The Fellowship offers an unparalleled opportunity to learn from and work collaboratively with US and international experts in medication safety to assess and develop global medication error-prevention strategies.

How to Apply

Information, a course outline, and an application can be found at:

www.ismp.org/sc?id=2898.

Applications can also be requested by calling 215-947-7797.

The application deadline for the International Fellowship is June 30, 2017.