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

Do not cut scopolamine or cloNIDine patches to deliver partial medication doses

Problem: A children's hospital reported two cases in which prescribers advised parents to cut a child's scopolamine or clo**NID**ine patch to provide a reduced dose of medication. However, neither patch should have been cut as this can impact the drug delivery rate and may result in patients receiving an increased dose due to additional drug leaking out from the reservoir. We wrote about similar events in our March 11, 2021 article, *Analysis of transdermal medication patch errors uncovers a "patchwork" of safety challenges*. Serious toxic effects are possible when a patch is cut and can result in a scopolamine or clo**NID**ine overdose. Details of the two recent events follow.

In the first case, a prescriber told a child's dad to use tape to cover three-quarters of a scopolamine transdermal system (patch) to provide a partial dose (i.e., one-quarter of a patch) to treat excess secretions. When the dad asked for clarification about how to tape it, the prescriber stated to cut the scopolamine patch instead and place one-quarter of the patch on the child. A statement on the back of the patch packaging says, "Do not cut the transdermal system" (**Figure 1**), but the small font size along with a lot of other text makes this warning easy to overlook. Once home, the dad cut and placed one-quarter of the patch behind his child's ear. Three hours later, he noticed the child was pursing her lips and having trouble swallowing. The dad became concerned that this was due to side effects from the scopolamine patch and removed it. Within a few hours, the child returned to baseline.

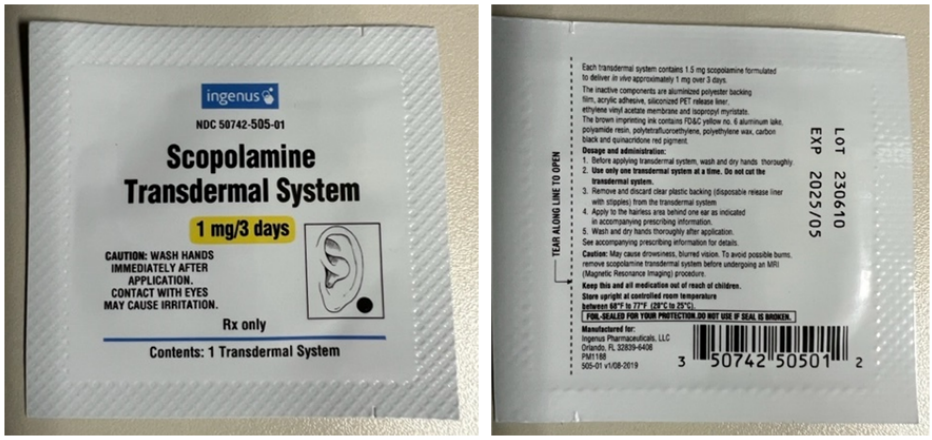

Figure 1. The back of the scopolamine patch pouch (right) states, "Do not cut the transdermal system." However, this is in a tiny font and buried within text, which makes it difficult to read. Also, there is no warning on the front of the scopolamine pouch (left).

In the second case, a prescriber ordered a clo**NID**ine transdermal system (patch) for a child to treat hypertension. The child's mom messaged the prescriber through a patient portal to notify them that her child was experiencing somnolence and bradycardia. The prescriber replied to the message, instructing the mom to cut her child's clo**NID**ine patch in half as a method to reduce the dose and lessen the side effects. The following morning, the prescriber sent a follow-up message, stating not to cut the patch in half, but instead to place tape over half of the patch to provide the reduced dose. However, the mom had already placed the cut patch on her child and was unaware the prescriber had sent a new message in the portal. The clo**NID**ine patch package does not include a warning to avoid cutting it (**Figure 2**, page 2).

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SAFETY briefs

Do not use unapproved EPINEPHrine nasal solutions. On January 16, 2025, the US Food and Drug Administration (FDA) issued a warning not to use **EPINEPH**rine nasal solutions manufactured by BPI Labs and Endo USA (labeled as **ADRENALIN** by Par Pharmaceuticals). These topical **EPINEPH**rine solutions were never FDA-approved. **NEFFY** (**EPINEPH**rine) is the only FDA-approved nasal spray indicated for anaphylaxis.

In addition, the similarities between the unapproved **EPINEPH**rine nasal solution bottle and packaging labels compared to the FDA-approved sterile injectable product (**Figures 1** and **2**, page 2) make it difficult to distinguish them from each other which can lead to practitioners accidentally injecting the non-sterile nasal solution instead of the injection product. Several reports of confusion between these products have been reported to FDA and ISMP.

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IMPORTANT! Read and utilize the Acute Care Action Agenda

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, selected items from the **October – December 2024** issues of the ***ISMP Medication Safety Alert! Acute Care*** newsletter have been prepared for use by 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. The **Action Agenda** is available for download as an Excel file.

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After approximately 24 hours, the mom saw the updated instructions, removed the cut patch, and applied a new patch with tape covering half. The child continued to experience somnolence and bradycardia, so the mom called the prescriber's office, and they instructed her to remove the patch. Unfortunately, the child's symptoms worsened over the next few hours. The parents drove the child to the emergency department (ED), but en route, the child became unresponsive to sternal rub, so they called 911. An ambulance met the parents and drove the child to the ED. He was admitted for observation and fortunately returned to baseline in less than 24 hours.

Figure 2. The front (left) and back (right) of the clo**NID**ine transdermal system package does not include a warning to avoid cutting the patch.

Alza, the manufacturer of the proprietary (brand) name product **CATAPRES-TTS** (clo**NID**ine), told us there is no indication that the Catapres-TTS patch can be cut and administered, nor that it can be used to deliver a partial dose. They noted that cutting, dividing, folding, or covering one portion of the patch to achieve lower incremental doses is not indicated according to the official labeling of the product and doing so could be hazardous since they do not know the exact amount of drug that will be absorbed and cannot predict the activity/behavior and efficiency of the patch if part of it is covered, folded, or cut.

Safe Practice Recommendations: We have notified the US Food and Drug Administration (FDA) to recommend that manufacturers of scopolamine and clo**NID**ine transdermal systems update the packages to include a prominent warning to not cut the patch. If patients require a dose less than what the full patch provides, organizations should consider if alternative dosage formulations or medications may be more appropriate. Review the prescribing information for patches on the formulary and follow the manufacturer's recommendations regarding the safety and efficacy of cutting patches. If a patch cannot be cut, build a warning, "Do NOT cut patch," into medication order sentences and outpatient prescriptions, and ensure this information is visible on the medication administration record and discharge instructions. When appropriate, consider restricting prescribers from being able to order partial dosages (e.g., similar to controlled release tablets, only allow them to order the entire dosage form). Educate practitioners and patients to ensure they are aware of which patches cannot be cut due to the impact on the drug delivery rate.

While it is clear that these patches should not be cut, we have heard that some organizations cover part of the patch using adhesive bandage or only remove half of the backing and cover the remainder with occlusive dressing prior to administration. This process is also risky, especially if asking patients or parents to do this at home. It is important to understand that the dressing could be accidentlly removed, or a child could touch and displace it, exposing a larger surface area of the patch, and increasing the risk of an overdose. In addition, clo**NID**ine manufacturers (e.g., Alza, Teva, Mylan, TruPharma, Dr. Reddy's, Mayne) do not have data to support covering a portion of the patch to provide an incremental dose, and it is unknown if the medication is evenly

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For these reasons, on December 20, 2024, Endo USA voluntarily recalled its unapproved Adrenalin nasal solution. FDA recommended that BPI Labs recall its unapproved **EPINEPH**rine nasal solution on December 12, 2024, but the company has not acted to remove it drug from the market.

Figure 1. BPI Labs unapproved **EPINEPH**rine nasal solution (left) comes in what looks like a parenteral injection vial similar to the FDA-approved **EPINEPH**rine injection (right).

Figure 2. Endo USA's unapproved Adrenalin (**EPINEPH**rine nasal solution) (left) comes in what looks like a parenteral injection vial similar to the FDA-approved Adrenalin (**EPINEPH**rine injection).

Organizations should not use unapproved **EPINEPH**rine nasal solutions. For additional information refer to the FDA alert. Please continue to report errors to ISMP and FDA.

HIGH-ALERT

Incorrect concentration of dextrose infusions prepared during shortage. During the current intravenous (IV) fluid shortage, a pharmacy technician inadvertently prepared bags of 70% dextrose instead of 5% dextrose. Because of the shortage and lack of availability of 5% dextrose, the technician was asked to compound 250 mL bags of 5% dextrose via an email communication from a pharmacy manager. The night before the event, the email was sent to select staff, including the technician, but not to the sterile compounding room pharmacist. When the technician arrived, he read the email communication which stated to prepare the 5% dextrose bags between 6 and 7 am, but the email did not provide adequate instructions. Neither the pharmacy manager nor the sterile compounding room pharmacist was available that early in the day, so the technician did not seek clarification before preparation.

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dispersed throughout the patch. If organizations are still considering covering a portion of a patch, we recommend completing a failure mode and effects analysis (FMEA) to determine potential failure points and mitigation strategies, and to monitor patients closely for side effects.

Provide order clarity when medications are to be given in divided doses

Problem: Ordering medications using a total dose that must be divided into multiple doses over a specific time period can be a complex and error-prone process. A hospital reported several safety events during which misinterpretations of recommended dosing regimens occurred. The problem was with medications, such as antibiotics or chemotherapy, that needed to be administered more than once in a given time frame (e.g., 3 doses given within a day or week). The hospital shared some recent examples that had common contributing factors, as well as recommendations for a safer, standardized dosing convention.

Recent Errors with Divided Doses

The first two reported errors involved intravenous immune globulin (IVIG):

- *An order for IVIG was entered as "2 g/kg dose for 2 days." However, in the consultant's notes, a recommendation to prescribe the IVIG was written as 2 g/kg divided over 2 days (1 g/kg/day each day for 2 days). The patient received the wrong dose (2 g/kg per dose on day 1 and day 2) before the error was recognized.*
- *A patient received divided doses of IVIG over 3 days, but the prescriber ordered "IVIG 95 g intravenously once, for 1 dose." Upon clarification, the intended dose was 95 g total, divided over 3 days (31.7 g each day for 3 days).*

Also, an error was identified with an outpatient prescription during an emergency department (ED) visit:

- *A patient presented to the ED with abdominal pain, nausea, bloating, and poor oral intake. These symptoms, including vomiting, had been going on for several weeks after the patient began taking* ***AUGMENTIN*** *(amoxicillin-clavulanate) at home. The patient had a prescription for "Augmentin 1,600 mg of amoxicillin component BID." Upon investigation in the ED, it was confirmed that the patient was receiving a total of 3,200 mg/day (1,600 mg twice a day) of amoxicillin instead of 1,600 mg/day divided into two daily doses (800 mg twice a day) of the amoxicillin component.*

An error also occurred when an order to taper a medication's total daily dose was confused with each dose:

- *A prescriber intended to decrease the patient's dose of hydrocortisone sodium succinate from 1.5 mg/kg/day, divided every 6 hours, to 1 mg/kg/day, divided every 6 hours. However, the prescriber entered the order as 1 mg/kg/dose every 6 hours. The patient received the wrong dose before the error was recognized.*

Tragic Example

The above examples reminded us of a highly publicized, tragic error that happened in the mid-1990s. The case involved Betsy Lehman, a 39-year-old mother of two, and a health reporter for the *Boston Globe*. Ms. Lehman was undergoing treatment for breast cancer and was hospitalized for her third round of chemotherapy. At the time, it was common for chemotherapy doses to be prescribed in inconsistent ways, even in the same hospital, with some prescribers ordering the total cycle (or course) dose to be divided over a set number of days, while others prescribed the daily dose. Ms.

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The typical morning workflow was for the technician to remove and discard the products (e.g., amino acids, 70% dextrose) on the automated compounding device from the previous day, and scan and set up the new products for use that day. The manager intended for the 5% dextrose bags to be prepared using the compounder, in an attempt to conserve the remaining dextrose 70% injection set up on the automated compounding device before it expired and was discarded. To do so, the sterile compounding pharmacist would need to generate automated compounding device labels with barcodes for the technician to scan prior to compounder use, but this had not been done. The pharmacy had an intravenous workflow management system (IVWMS), but 5% dextrose infusion labels were not sent via the IVWMS workflow. Instead, the technician generated 5% dextrose labels from a shared drive template, and, thinking the dextrose bag that was hanging on the compounder was 5% dextrose, manually prepared straight 70% dextrose into empty sterile bags. After arrival, the sterile compounding room pharmacist saw the bags labeled 5% dextrose and asked the technician what she was checking since no compounding preparation instructions were provided. The technician forwarded the manager's email to the pharmacist which stated to use 70% dextrose to prepare 5% dextrose bags, so the pharmacist thought that dextrose 5% had been compounded, and signed off on the preparations.

The 70% dextrose bags that were labeled 5% dextrose were dispensed to the cancer center pharmacy. Three days later, the technician returned to work in the sterile compounding room, read the label on the dextrose bag set up on the automated compounding device, and recognized that the product he had used 3 days prior was actually 70% and not 5% dextrose. Fortunately, the mislabeled bags were not administered to any patients and were discarded.

Hypertonic dextrose (20% or greater) is considered a high-alert medication. Administration of dextrose at a rate exceeding the patient's tolerance can cause hyperglycemia associated with an increase

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Lehman was supposed to receive cyclo**PHOS**phamide 1 g/m^2 each day (1,630 mg) for a total of 4 days. That should have been 6,520 mg infused over the 4-day period. However, the drug was ambiguously ordered in a total cycle dose as "4,000 mg/m^2 x 4 days." Unfortunately, she received 6,520 mg of cyclo**PHOS**phamide *each day* for 4 days (a total of 26,080 mg)! Multiple system failures occurred, and human double checks failed. Lehman died from the toxic dose before being discharged from the hospital.

Ms. Lehman's death was widely publicized nationally and internationally. In turn, her case contributed to the Institute of Medicine's investigation into medication errors and the eventual publication of *To Err is Human*. The chemotherapy error catalyzed a lasting movement to improve patient safety and reduce medication errors. The oncology community in the United States specifically took the Lehman incident to heart, with intense introspection that led to many systematic changes to improve safety. For example, we rarely see chemotherapy regimens ordered as the total cycle dose. In fact, the ***ISMP International Medication Safety Self Assessment for Oncology*** has an item that states, "Writing the total chemotherapy/biotherapy dose for the entire cycle of treatment is prohibited (e.g., order should be written as 400 mg/m^2 on day 1, 2, 3, and 4, not as 1,600 mg/m^2 over 4 days)."

Safe Practice Recommendations: Prescribing information, drug information resources, organizational protocols/order sets, as well as individual practitioners, have inconsistently communicated dosing conventions, particularly for medications that need to be administered more than once over a given time frame. The US Food and Drug Administration (FDA) should require manufacturers to avoid using "divided" doses in the prescribing information and organizations and individual practitioners should avoid writing orders in terms of total doses that would be divided over a period of time. Instead indicate the individual dose followed by the frequency of administration. For example, prescribe "5 mg/kg every 12 hours," not "10 mg/kg/day in divided doses every 12 hours." Organizations should review order sentences and dosing guidelines to make sure each single dose and frequency are clear. It should also be clear when the medication dose will be stopped for medications which are tapered or used for a short duration. Use clinical decision support (e.g., dose range checking, dose error-reduction systems) to alert practitioners if a single dose is outside of the typical range.

Special Announcement

Virtual MSI workshop

Join us for our first ***ISMP Medication Safety Intensive (MSI)*** workshop in 2025. This unique 2-day virtual program will be held **March 13 and 14, 2025**. For more information and to register, please click here.

ASPEN parenteral nutrition practice survey

The American Society for Parenteral and Enteral Nutrition (ASPEN) is conducting a survey on current parenteral nutrition (PN) practices in the United States. US-based clinicians who are involved in the PN use process can participate in this survey, which takes 15 minutes to complete. We appreciate your participation in helping inform an update to the ASPEN PN guidance.

To subscribe: www.ismp.org/ext/1367

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in serum osmolality, resulting in osmotic diuresis, dehydration, and electrolyte losses, which may lead to coma and/or death.

As discussed in our October 17, 2024 article, *Weathering the storm—Safety considerations during fluid shortages, as organizations implement fluid conservation strategies that work best for their institution*, recognize that any change to compounding procedures or workflows may increase the risk of error. As a reminder, we recommend evaluating all systems impacted by workflow or product changes due to shortages. Communicate changes to policies and practices, systems, and workflow to all staff, and provide them with the opportunity (e.g., huddles) to ask questions and provide feedback about potential safety concerns. Use automated compounding devices and IVWMSs with video or images and/or gravimetric verification when manipulating or compounding all products. Ensure all compounds contain preparation instructions in the master formulation records. Provide pharmacy personnel with competency assessments related to impacted technologies (e.g., automated compounding device, IVWMS) and processes (e.g., preparing and checking a compounded sterile preparation). For additional information, refer to the ISMP ***Guidelines for Sterile Compounding and the Safe Use of Sterile Compounding Technology***. Empower staff to "stop the line" and ask questions when safety concerns arise. Report medication errors, close calls, and hazards, including those related to shortages, to ISMP. Share lessons learned within your organization and externally with others.

We turned 30!

The ***ISMP Medication Safety Alert! Acute Care*** newsletter recently reached 30 years of publication! Its look and delivery method have changed over time, but its mission has not. It has grown to be the leading source of real-time medication error information and prevention recommendations, read by millions of healthcare professionals and reaching nearly every US hospital. For more on ISMP's newsletters, click here.