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ISMP

Community/Ambulatory Care

ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Preventing 10-fold dosage errors

Mix-ups in prescribing and dispensing between available drug strengths that differ by a factor of 10 have been a common cause of error. For example, we've previously published reports about errors with **ABILIFY** (**ARIP**iprazole), which is available in 2 and 20 mg tablet strengths, and predni**SONE**, available in 5 and 50 mg tablet strengths. We encourage pharmaceutical companies and the US Food and Drug Administration (FDA) to avoid developing and approving dosage strengths that differ by a factor of 10 because they contribute to medication errors.

The latest reported error occurred with **BELBUCA** (buprenorphine), which is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The drug is available as a buccal film in **75**, 150, 300, 450, 600, **750**, and 900 mcg strengths. We recently heard from a consumer regarding an incident in which her pharmacy dispensed 750 mcg instead of 75 mcg, which is the recommended starting dose. It is unknown whether the prescription was handwritten or typed and whether or not there was a trailing zero involved (i.e., 75.0 mcg). It is also possible that the 75 and 750 mcg strengths may have appeared next to one another in a drug drop-down list. The patient took 5 doses of the erroneous 750 mcg strength. She experienced pain relief but was unable to stay awake and experienced dizziness, lightheadedness, and vomiting. She contacted her doctor to tell him that she was unable to tolerate the medication and learned that he had prescribed 75 mcg, not 750 mcg.

The risk of 10-fold overdoses is increased by health professionals and computer systems that dangerously use trailing zeros (e.g., 1.0 mg, which can be misread as 10 mg), or by healthcare workers who do not use leading zeros (e.g., .5 mg instead of 0.5 mg, the former of which can be misread as 5 mg). All too often, blame is cast upon prescribers

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PUT YOUR BOOTS ON ...

Join ISMP on Tuesday evening, **December 6, 2016**, at 6:00 pm for the 19th **Annual Cheers Awards**, at **Stoney's Rockin' Country** in Las Vegas! Each year, ISMP celebrates individuals and organizations that have set a standard of excellence in the prevention of medication errors during the previous 12 months. This year's **Keynote Speaker** will be **Daniel Budnitz, MD, MPH, CAPT. USPS**, Director of the Medication Safety Program at the US Centers for Disease Control and Prevention (CDC). The **Lifetime Award** will be presented to **David Marx, JD**, CEO of Outcome Engenuity, a true pioneer in the safety world, and father of the Just Culture accountability model. To register for the awards dinner or to make a donation to ISMP, please visit: www.ismp.org/Cheers/. We hope to see you there!

NANALERT

Syringe leakage. An alert was distributed earlier this month through the National Alert Network (NAN) asking clinical and technical healthcare staff to look for fluid leakage during the syringe-filling process. The alert was issued after the ISMP National Medication Errors Reporting Program (ISMP MERP) received reports of medication leaking beyond the syringe plunger onto surfaces exposed to air. The leaks happened most frequently when the plunger and barrel were not vertically aligned while filling the syringe. Leakage has occurred with both hazardous and nonhazardous drugs. The reports included syringes of various sizes and were manufactured by BD. However, BD has determined the 10 mL syringe is most affected and a correction is underway. ISMP recommends discarding syringes with fluid that has leaked past the black stopper on the plunger, as contents may be potentially contaminated or pose a risk to workers. Additional precautions to avoid contamination of work surfaces and exposure to personnel are required if leaking syringes contain hazardous drugs. The alert, which provides additional information and recommendations, is available at: www.ismp.org/sc?id=2811.

SAFETY briefs

HIGH-ALERT

An EPIPEN replacement idea that's likely to lead to dosing errors. We have been happy to see the media coverage of the exorbitant pricing of Mylan's EpiPen (**EPINEPH**rine autoinjector) and how it might be contributing to patients going without this life-saving medication as well as serious medication errors. What we weren't happy about, though, were some of the short-term, cost-saving recommendations that accompanied the me-

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Worth repeating...

RisperiDONE and rOPINIRole mix-ups

RisperiDONE 0.25 mg orally every evening was prescribed for a patient who suffered from oppositional defiant disorder. In error, the pharmacy dispensed rOPINIRole 0.25 mg. The patient's grandmother called the doctor to say the medication wasn't working and was making the patient worse, with non-stop wild behavior and uncontrollable laughing. RisperiDONE was increased to 0.5 mg, and this time the pharmacy dispensed the correct drug. Later, in a therapy session, the grandmother brought in the medication bottle, which was labeled rOPINIRole. All medications were prescribed electronically, and medication records and reconciliation indicate that risperiDONE 0.25 mg was the drug prescribed and electronically transmitted. It was later confirmed that the pharmacy had dispensed the wrong medication.

RisperiDONE (RISPERDAL) is an antipsychotic agent while rOPINIRole (REQUIP) is a dopamine agonist used in Parkinson's disease and restless legs syndrome. There's a long history of mix-ups between these drugs. We published a previous "Worth Repeating" in August 2014 when a patient experienced difficulty sleeping and involuntary movements in her extremities after taking what was thought to be rOPINIRole 0.5 mg but was actually risperiDONE 0.5 mg tablets. The US Food and Drug Administration (FDA) warned the public about confusion with this name pair in 2011 after reviewing over 200 errors sent to ISMP and the FDA Adverse Event Reporting System (www.ismp.org/sc?id=1684). Some patients required hospitalization. FDA asked manufacturers to use tall man lettering on container labels and carton packaging (risperiDONE, rOPINIRole) to help distinguish between the two products, and this may be helping. The number of error reports sent to FDA and ISMP has decreased markedly since 2011, although electronic prescribing is likely playing a role, too.

Other causes of confusion with this similar drug name pair include illegible, handwritten prescriptions; similar strengths, dosage forms, and dosing intervals; proximity of storage; appearance of product names together in computer listings; and look-alike container labels if the same company manufactures both products. By addressing these known causes of confusion, you can minimize the risk of an error. When prescribing either drug, the purpose should be included. In pharmacies, the products should not be stored near each other, and tall man letters should be used for storage, computer listings, and labels (except for patients).

Special Announcements

ASHP and ISMP to Create Medication Safety Certificate Program

The American Society of Health-System Pharmacists (ASHP) and the Institute for Safe Medication Practices (ISMP) are partnering to develop a **Medication Safety Certificate Program** that is scheduled to launch in Spring 2017. This online continuing education (CE) certificate program will be an addition to ISMP's Medication Safety Intensive program. More information is available at: www.ismp.org/sc?id=2801.

ISMP Medication Safety Intensive

Join your colleagues at the ISMP **Medication Safety INTENSIVE (MSI)** workshop on **December 2-3** in **Las Vegas, NV** or one scheduled in 2017. For more information and to register, please visit: www.ismp.org/sc?id=637.

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dia attention. In one news story it was suggested that, instead of paying for an EpiPen or generic EPINEPHrine pen, an EPINEPHrine anaphylaxis treatment kit could be prepared using an empty Altoids tin (**Figure 1**) or toothbrush container, a 1 mg EPINEPHrine ampul or vial, a plastic syringe, a needle, and an alcohol pad, all for about $10 (www.ismp.org/sc?id=2799).

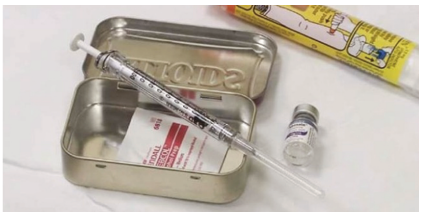

Figure 1. This unsafe, make-shift anaphylaxis treatment kit includes a 1 mg vial of EPINEPHrine (see link above for source).

We were also alerted to a YouTube video (www.ismp.org/sc?id=2813) that promoted a homemade EPINEPHrine autoinjector which could be assembled for about $30.

The EpiPen delivers a 0.15 mg dose for children and a 0.3 mg dose for adults. There is 1 mg of EPINEPHrine in each ampul or vial. We have received reports in which experienced health professionals have accidentally given the entire 1 mg of EPINEPHrine in the vial instead of the proper dose (0.1 mg) intramuscularly (or even intravenously when a patient had an IV line in place).

Given the life-threatening nature of anaphylaxis, any episode has to be extremely stressful and anxiety-provoking for a caregiver. Even when training and written instructions have been provided in advance, that knowledge may be lost over time. There's every reason to expect wrong dose errors, particularly overdoses, will happen when a parent or caregiver uses the ampul or vial. It's certainly possible this could lead to significant adverse effects for a child, so we can't recommend that EPINEPHrine anaphylaxis treatment kits or homemade autoinjectors be provided as an alternative, even if it is a cost-saving measure.

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and pharmacists for prescribing or dispensing errors when many of these would not occur if companies took a safer approach of testing and marketing medications with strengths that are above or below an exact 10-fold difference. We saw this change when fenta**NYL** transdermal was marketed in a 12.5 mcg/hour dosage form. The manufacturer, Janssen, labeled it **DURAGESIC-12** in an attempt to prevent mix-ups between Duragesic 12.5 mcg/hour and Duragesic 125 mcg/hour (requiring 100 mcg/hour and 25 mcg/hour patches), which may be an acceptable dose for opioid tolerant patients with chronic pain. Manufacturers and the drug approval divisions at FDA should take note of this as they contemplate drug approvals, especially for high-alert medications. For example, why not Belbuca 700 mcg or 740 mcg?

T for two (or maybe 5)

Over the last few years the US Food and Drug Administration (FDA) has approved many new products to improve blood sugar control in adults with diabetes. Five of these newly approved medications have a few things in common. Four are long-acting injectable pens, three are indicated for type 2 diabetes, BUT all five of these begin with the letter "T."

- **TRADJENTA** (linagliptin), a dipeptidyl peptidase-4 (DPP-4) inhibitor, is an oral tablet indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- **TRULICITY** (dulaglutide) injection, a glucagon-like peptide-1 (GLP-1) receptor agonist, is a once-weekly injectable prescription medicine to improve glycemic control in adults with type 2 diabetes mellitus.
- **TANZEUM** (albiglutide) for injection, also a once weekly GLP-1 receptor agonist, is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- **TOUJEO SOLOSTAR** (insulin glargine) pen, a long-acting insulin, is available in a 300 units/mL concentration for adults with diabetes who have taken insulin and for those who haven't. Its release is gradual to provide stable insulin levels for a full 24 hours and beyond.
- **TRESIBA FLEXTOUCH** (insulin degludec) pen is a long-acting insulin for adults with diabetes and is available in 2 concentrations: 200 units/mL and 100 units/mL.

Although we have not received any error reports detailing mix-ups among these products, pharmacists have expressed concerns in discussions at professional meetings. It would not surprise us if there will be name and strength confusion with these products. Be proactive and assess how these products are displayed and selected in your computer system. Evaluate where and how these products are stored. Take steps to differentiate names and concentrations on computer screens and product packaging. Provide patient counseling at the point-of-sale and include a review of the product with the patient.

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HIGH-ALERT

Misuse of new insulin strengths. Education is important for both patients and health practitioners regarding the new higher concentration insulin products that are available only in a pen, including U-300 **TOUJEO** (insulin glargine), U-200 **TRESIBA** (insulin degludec), and U-200 **HUMALOG** (insulin lispro). U-500 insulin is also available in a pen (**HUMULIN**), but vials remain on the market. Patients may not understand proper dosing and dose measurement with these new products.

A patient who was previously using **LANTUS** (insulin glargine) U-100 was switched to Toujeo U-300. He was given pen needles to use with Toujeo, but at home, he decided to use the insulin pen cartridge as a vial. He drew up a dose with a leftover U-100 syringe, filling it to the 100 unit mark, the same daily Lantus dose he had been taking. This resulted in a dose of 300 units of Toujeo, which led to hypoglycemia requiring hospital admission.

With U-500, not only is there a risk of an overdose, but underdosing is also possible. In the past, many patients using vials of U-500 insulin measured their dose with a U-100 syringe but used the syringe scale to measure only 20% of the actual dose. For example, 40 units on the U-100 syringe scale is 200 units of U-500 insulin. If patients now use the new U-500 pen and dial only the number of units they previously measured (40 units), the patient would receive only one-fifth of the prescribed dose. With the various high concentration insulin products now available in pens, it is important to warn both patients and health professionals about these new risks.

ISMP INSTITUTE FOR SAFE MEDICATION PRACTICES

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Report medication and vaccine errors to ISMP: Call 1-800-FAIL-SAF(E), or visit www.ismp.org/MERP or www.ismp.org/VERP. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

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ISMP AmbulatoryCare ActionAgenda

ISMP 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 agenda items have been prepared for you and your staff to stimulate discussion and collaborative action to reduce the risk of medication errors. These agenda topics appeared in the *ISMP Medication Safety Alert!* Community/Ambulatory Care Edition between May 2016 and August 2016. Each item includes a brief description of the medication safety problem, recommendations to reduce the risk of errors, and the issue to locate additional information. The Action Agenda is also available for download in a Word format at: www.ismp.org/Newsletters/ambulatory/actionagenda.asp. To learn how to use the ISMP Ambulatory Care Action Agenda at your practice site, visit www.ismp.org/newsletters/ambulatory/How_To_Use_AA.asp.

Key: ⚠ – ISMP high-alert medication

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Prescribing and dispensing errors with oral solutions					
05/16 ⚠	A 3-month-old infant was hospitalized with a respiratory infection. The parents said she had been receiving 8 mL (800 mg of a 100 mg/mL solution) of **KEPPRA** (lev**ETIRA**cetam) every 12 hours prior to admission for a seizure disorder. A pediatric resident prescribed the same dose without noticing that it was excessive. A pharmacist following up on the dose learned that the baby had been receiving the correct dose of 80 mg every 12 hours after birth, but after a prior admission and discharge, had been receiving "8 mL" of medication for each 12-hour dose.	Express single-entity drug doses in metric weight, not volume alone. Add weight-based and calculated doses on orders and prescriptions, and include the patient's age/date of birth and weight (in metric units) on prescriptions. Build alerts to warn prescribers and pharmacists about unsafe doses. Test the alert system periodically, and ensure that the dose alerts are enabled and not bypassed easily without documentation. Educate patients and require the patient/parent/caregiver to demonstrate proper dose measurement of all liquid medications for pediatric patients.			
Risk with entering a "test order"					
08/16	Submitting a contrived prescription to a patient's pharmacy to determine insurance coverage has led to close calls and actual dispensing of the medication to the patient. For example, when a nurse was following-up on a warfarin refill request, she noticed that both apixaban and warfarin were on the patient's medication list. Review of electronic health record (EHR) notes discovered a "test script" for apixaban had been sent to the pharmacy to determine the copay. The prescription was dispensed and the patient received both medications for 3 days, luckily without harm, before the error was discovered. A similar situation occurred with warfarin and rivaroxaban.	Educate prescribers that sending "test orders" to pharmacies to determine insurance coverage or copays is dangerous. Prescribers should maximize the use of their EHR's ability to access a patient's health plan formulary information as well as submit prior authorization requests directly to the health plan electronically before transmitting a prescription to the pharmacy. If this functionality is not currently available in the application, plan for EHR upgrades to implement these functions. Otherwise the patient, prescriber, or a prescriber-designated individual should call the insurance company or pharmacy benefits manager (PBM) to inquire about coverage before transmitting the electronic prescription to the pharmacy.			

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Vaccine errors associated with age-related factors					
08/16	Vaccine errors can leave patients unknowingly unprotected against preventable diseases. Age-related contributing factors were reported most often and were linked to more than 1 in every 3 error reports (38%). The age-related errors were often due to confusion between numerous age-dependent vaccines that target the same disease, unfamiliarity with the vaccine specific recommended age, or not verifying the patient's age prior to administration. Similar packaging and labeling also contribute to vaccine errors.	Purchase age-specific formulations from different manufacturers. Store vaccines with similar labels, names, or overlapping components separately from one another. Separate pediatric and adult formulations of vaccines in storage areas. Use auxiliary warning labels to draw attention to vaccines which come in multiple formulations. Post immunization schedules in clinical areas where vaccines are given, and prior to prescribing, dispensing, or administering a vaccine, verify the patient's age. Discuss vaccine errors that can occur and how to prevent them with health professionals who prescribe, dispense, and administer vaccines.			
Avoid the directions "use as directed"					
07/16	Based on a survey ISMP conducted from May 19 to June 19, 2016 targeting outpatient pharmacies, many drugs are still prescribed and dispensed with the ambiguous directions "use as directed." Errors have occurred when two drug names look or sound similar and the pharmacist chooses the incorrect product, not knowing how it is to be used. Other errors happen when there are inadequate directions for use on the prescription label and the person administering the medication has not been properly educated.	Prescribers should include explicit directions for use on prescriptions including the strength, frequency of administration, route of administration, and duration of therapy. Pharmacists should clarify the directions for use with the prescriber when they receive a prescription with the sig "use as directed." If the directions exceed available space on the pharmacy label, a supplemental or overflow label may be required. Teach patients about the medication and assess their ability to take the medication correctly.			
New syringe and package insert for HUMULIN R U-500					
08/16 ⚠	Many medication errors have occurred when using U-100 or tuberculin syringes to administer U-500 insulin due to confusion and conversion errors. A new U-500 syringe designed for the administration of regular insulin (concentrated) U-500 will be available later this year. It has a volume of 0.5 mL with a scale measuring from 25 to 250 units in 5 unit increments. A new package insert has also been published for Humu**LIN** R U-500 (www.ismp.org/sc?id=2786).	Once the U-500 syringe is available, no longer prescribe or dispense U-100 or tuberculin syringes to administer U-500 insulin. Co-prescribe the U-500 syringes with U-500 insulin vials (unless the prefilled pen is prescribed). Prescribers will need to order U-500 insulin in actual units of U-500 rather than expressing the dose in terms of U-100 units to facilitate use of a U-100 syringe. Educate patients and make sure they can accurately prepare and administer a dose.			

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Methotrexate-metOLazone mix-ups					
06/16 ⚠	Two errors occurred in which methotrexate was dispensed instead of met**OL**azone, resulting in the death of a patient. In the fatal error, a nurse called prescriptions into the pharmacy, and met**OL**azone 2.5 mg daily was transcribed incorrectly as methotrexate 2.5 mg daily. In the other error, a prescription was entered into the pharmacy computer as methotrexate, and the checking pharmacist did not compare the label to the original order.	Segregate methotrexate from other medications in the pharmacy, employ a hard stop in dispensing software to prevent "daily" instructions on the label, and educate the patient about weekly dosing. A methotrexate patient counseling handout is available in English and Spanish on our website (www.ismp.org/sc?id=1709). Also, pharmacists should always check the original prescription when verifying order entry and/or the final product.			
Opioid sharing, storage, and disposal					
06/16 ⚠	Results of a national survey examining practices surrounding the sharing of opioids and medication storage and disposal (Kennedy-Hendricks A, et al. *JAMA Internal Medicine.* 2016.) indicated that 20% of respondents had shared opioid medications with another person. Over 60% of respondents with left over opioids kept them for future use, and almost half of respondents did not recall receiving information on safe storage or proper disposal.	Avoid prescribing large quantities of opioids and better communicate the risks involved with opioid therapy and ways to safeguard use, storage, and proper disposal. Patient education about opioids should be mandatory and scripted. Use ISMP's free high-alert medication consumer leaflets for selected opioids (www.ismp.org/sc?id=1709) during patient education sessions.			
Don't squeeze the round DROP-TAINER					
05/16	Patients reported running out of latanoprost ophthalmic solution early. The patients were using the medication according to the pharmacy label instructions, but they were squeezing the round Drop-tainer bottle causing variability in dosing. Patients must press the bottom of the round Drop-tainer bottle rather than squeeze it, which is done for other bottles.	Pharmacist should identify products dispensed in Drop-tainer bottles, particularly the round versions. Ensure patients are educated on proper administration technique and verify that they can correctly administer the medication. Manufacturers should include clear instructions for proper use in the product labeling.			
New brand name for vortioxetine					
05/16 ⚠	Because of mix-ups between the confused drug names **BRINTELLIX** (vortioxetine) and **BRILINTA** (ticagrelor), the name Brintellix has been changed to **TRINTELLIX**. Due to the lag time associated with manufacturing bottles with the new brand name, you may continue to see bottles labeled with the brand name Brintellix during the transition period.	Pharmacy staff who order and stock the medication should be aware that Trintellix will have a new National Drug Code (NDC) number. Drug information and electronic system vendors should start using the new brand name and NDC number. Including the purpose on prescriptions for either drug can help prevent mix-ups.			