**Problem:** In our February 7, 2013 newsletter, ISMP suggested that hospitals strongly consider transitioning away from insulin pen use in the acute care setting, with a few exceptions (www.ismp.org/sc?id=161). Given reports of ongoing misuse of insulin pens—in particular, the sharing of insulin pens with multiple patients after only changing the needle, as well as needlestick injuries, user technique errors, and pen design flaws as first described in 2008 (www.ismp.org/sc?id=160)—we believe the risk associated with cross-contamination is best mitigated by removing insulin pens from use in hospitals.

While we stand firmly behind our recommendation on this issue, we want to take this opportunity to point out that simply replacing insulin pens with insulin vials may result in unintended vulnerabilities that can result in errors.

First, for staff who have been using insulin pens for any length of time, transitioning back to insulin vials may uncover knowledge deficits that may lead to errors and patient harm. Edrees et al. described such an event in 2011. A physician had ordered a “stat” dose of insulin aspart 10 units IV along with a dextrose infusion to treat a patient with hyperkalemia. Several years before, the hospital began using insulin pens. Since graduation, the nurse who needed to give the insulin had only used the pens and had forgotten that only insulin syringes should be used when measuring an insulin dose from a vial. She felt stressed to give the insulin quickly and called the pharmacy for assistance. The pharmacist advised her to use the vial of insulin aspart from the medication refrigerator. The concentration and total dose was not readily apparent on the vial label. She showed the vial to another nurse, who confirmed it was the right medication. The younger nurse thought the other nurse had confused the entire vial contained the required dose. She withdrew all 10 mL of the 100 units/mL insulin into a 10 mL syringe and administered 1,000 units intravenously. Fortunately, the error was quickly recognized and the patient was treated to avoid harm.

Second, even staff who can easily remember how to withdraw an insulin dose from a vial may encounter difficulties that result in unsafe insulin administration. Thus, there are safety issues with the use of insulin vials that must be addressed when transitioning away from insulin pens. What follows is a discussion regarding the most common safety issues associated with insulin vials along with recommendations to lessen the risk of medication errors during this transition in the acute care setting.

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**Tretinoin confused with ISOtretinoin**

A 14-year-old girl diagnosed with acute promyelocytic leukemia (APL) was started on oral tretinoin (all-trans retinoic acid [ATRA]) for induction therapy. APL is a medical emergency with a high rate of mortality, so it is critical to start treatment with tretinoin without delay as soon as the diagnosis is even suspected. The patient was hospitalized during treatment. She suffered from APL differentiation syndrome and pseudotumor cerebri such that doses had to be held and reduced, but she was able to finish the treatment course and achieved complete remission.

The patient was discharged, and the following month, she returned to the outpatient infusion center to begin 10 continued on page 4 — Confused
Searching for medication names during order entry. An unfortunate yet common issue that comes up during computer order entry is inadvertently picking the wrong drug from a drug name search list. For example, a prescriber may wish to enter an order for acetaminophen by typing “aceta,” but then accidentally choose acetazOLAMIDE from the search results. In a recent case, that very error was recognized by the processing pharmacist because the dose and frequency did not seem suitable for acetazOLAMIDE. Some of the other drug name pairs that have led to this kind of error are: 1) hydroxychloroquine/hydroxyurea, 2) MUCOMYST (acetylcysteine)/MUCINEX (guaifenesin), 3) valACYclovir/valGANeclovir, and 4) penicillinAMINE/penicillin. This type of error happens because the first portion of the generic or brand names for different medications are identical. When only a few letters of the drug are entered into the search box, the prescriber is often presented with a menu of choices and may quickly choose the medications that appear at the top of the browser. Steps to minimize this selection error include visually enhancing the letter character differences with tall man letters and requiring typing as much of the drug name as possible when searching, rather than just a few letters. (Some order entry systems require users to type a certain number of letters before a list appears.) For prescribers and pharmacists, double-checking the choices that are in the order entry browser, being familiar with the usual dosing and frequency of the intended drug, or checking references can also help. This process is all the more important as these look-alike medications sometimes have similar strengths, although most have very different indications. Requiring entry of the intended purpose of drugs with similar indications or building an alert for the pharmacist to verify that the indicated use matches the patient’s condition provide additional safeguards. It is often difficult for other caregivers, such as the pharmacist and nurse, to catch a prescribing error or unintended use in the absence of readily available access to the condition for which the drug is being prescribed.

Reduce Ambien dose in order sets. When reviewing your electronic or preprinted order sets, be sure to keep in mind that

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Dosing errors. With insulin, it should not be assumed that all healthcare professionals are knowledgeable and skilled when it comes to measuring doses and recognizing doses that exceed safe limits. For example, the U-100 designation on insulin vials has been misunderstood to represent 100 units per vial, leading to 10-fold overdoses. Taking into consideration that the label of virtually every other injectable drug notes both the “per mL” and “per total volume” amounts, one can understand how this inconsistency might contribute to such an error with insulin. The availability of 10 mL vials of insulin make very large overdoses possible. Another error that occasionally occurs is that the dose in units has instead been measured in mL (4 mL vs. 4 units) using a syringe with mL increments. Errors of this type suggest that some healthcare professionals do not fully understand the differences between an insulin syringe and other parenteral syringes. Adding to the risk of dosing errors is insulin’s availability in two concentrations (U-100 and U-500), whereas insulin syringes are best suited to measure the most common concentration (100 units/mL).

Look-alike vials. Some manufacturers have crafted distinctive labeling to help reduce confusion between various types and concentrations of the insulin they manufacture. However, ISMP still receives reports of serious mix-ups between insulin types and concentrations, and between insulin and other medications in similar-looking vials. For example, a patient recently received 1,000 units of LANTUS (insulin glargine) IV instead of PROTONIX (pantoprazole). A nurse had removed the vial cap and reconstituted Protonix with 0.9% sodium chloride as directed. She was momentarily distracted and, when returning to the task, she accidentally picked up a nearby vial of Lantus that also had its cap removed, which looked very similar to the Protonix—both vials have a distinctive, elongated shape. She withdrew and administered all 10 mL of Lantus. To cite another example, similar labeling of insulin and heparin in 10 mL vials and the fact that both drugs are dosed in units has contributed to mix-ups.

Unlabeled syringes. Insulin doses drawn into a syringe in patient care areas run the risk of being unlabeled. Even if the health professional intends to administer the dose immediately, interruptions are common and often result in delays in administration, leading an unlabeled syringe in drug preparation areas available to use in error.

Beyond use expiration dating. Healthcare professionals may forget to document an expiration date on an insulin vial once it has been punctured. Or, staff may not discard the vial upon the expiration date, thus allowing use of a product that may no longer be safe or fully potent.

Cross-contamination. The risk of a healthcare professional using the same insulin syringe and needle to draw up and administer insulin to multiple patients is extremely low, particularly given that most insulin syringes come with a permanently attached needle that cannot be changed between uses (changing needles is never enough to prevent cross-contamination). Further, while a 2010 survey revealed an alarming lapse of basic infection control practices associated with the use of syringes, needles, and multiple-dose vials, insulin is not as vulnerable to cross-contamination compared to a drug which often requires multiple entries into the vial to treat a single patient, such as lidocaine. (When multiple entries into a vial are required to treat a single patient, a mental lapse could result in using the same syringe and needle—because it is used for the same patient—thereby contaminating the product.) However, anytime multiple-dose vials are used, the risk of contamination is present.

In addition to these safety issues, it takes more time to prepare insulin doses from a vial than from a pen. Also, waste may be an issue if 10 mL vials are dispensed for individual patients.

Safe Practice Recommendations: When transitioning away from insulin pen use in hospitals, consider these recommendations to reduce the risk of errors.

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the US Food and Drug Administration (FDA) is requiring manufacturers that make zolpidem (AMBEN and generics) to lower the approved doses of the drug. If the drug is listed on order sets, you should make sure the dose is adjusted accordingly. Last month, FDA told manufacturers to lower the dose in light of new data showing blood levels in some patients may be high enough the morning after use to impair activities that require alertness, including driving. The FDA has informed the manufacturers that the recommended dose of zolpidem for women should be lowered from 10 mg to 5 mg for immediate-release products and from 12.5 mg to 6.25 mg for the extended-release product, AMBIEN CR. For men, FDA has informed the manufacturers that the labeling should recommend that healthcare professionals consider prescribing these lower doses (5 mg for immediate-release products and 6.25 mg for extended-release products). We realize most inpatients won’t be driving the next morning after hospitalization, but that circumstance is not out of the realm of possibility if the patient is discharged the morning after receiving zolpidem. Complex sleep-related behaviors, such as sleep-walking and sleep-driving (driving while not fully awake, and with no memory of the event), have been reported with zolpidem. CNS medications in general can add to or cause confusion, agitation, and delirium. Sleep medications may also increase the risk of a fall, especially in the presence of other risk factors such as advanced age. So, it seems prudent to heed the label updates for the dosing of this drug.

Don’t confuse levothyroxine with liothyronine. A child diagnosed with congenital hypothyroidism had been receiving levothyroxine (T4; SYNTHROID) for the first year of life with adjustment of his medication as necessary. At around 14 months, the child had significantly abnormal laboratory values with what appeared to be a central hypothyroidism profile (low TSH, low free T4). It took many months to figure out that the pharmacy was dispensing liothyronine (T3; CYTOMEL) instead of levothyroxine, causing the child to develop a significantly elevated T3 level (greater than 500 nanogram/dL). Liothyronine is much more “potent” than levothyroxine. The pharmacist on duty the day the error was noticed reported that the prescription was written as “L-thyroxine,” which apparently was confused as liothyronine (T3). These two drugs are similarly named, and several references warn against confusion. Consider adding an alert detailing the potency difference between these drugs in your order entry system.

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Re-educate staff. Before transitioning away from insulin pens, alert all clinicians to the change and re-educate staff regarding the processes associated with using insulin syringes, preparing doses (e.g., rolling insulin syringes or vials between the hands to mix suspensions), measuring doses, and injection techniques (e.g., pen needles usually do not require pinching of the skin prior to injection while traditional insulin syringe needles are typically longer and require pinching of the skin). Don’t assume all staff will recall these procedures correctly without review. Conduct initial training and verify competencies before making a change.

Dispense from pharmacy. To preserve an independent double-check, wherever possible, pharmacy should prepare, label, and dispense patient-specific insulin doses in insulin syringes, particularly for basal and other long-acting insulin. For rapid-acting insulin that is not dispensed in unit dose syringes, provide a vial of insulin—preferably a 3 mL vial—labeled for a specific patient. Labeling by pharmacy should make it clear that the 3 mL vial is a multiple-dose, not single-dose, vial from which the patient’s dose should be measured. This will help to avoid errors that might be caused by unfamiliarity with the 3 mL vial size, which might be new at your institution.

Stock the smallest vials. Consider stocking patient care units and treatment kits (e.g., hyperkalemia kit) that require rapid-acting insulin with 3 mL vials of insulin to reduce the risk of catastrophic dosing errors. (Although 3 mL of insulin represents a catastrophic overdose, the risk of a massive overdose is lessened with each correct dose removed from the vial.) Ideally, the hyperkalemia kit would include insulin syringes as part of the kit so that they are readily available. The kit might also prominently display the fact that 10 units = 0.1 mL, a typical dose to treat hyperkalemia (for adults). This may also decrease the possibility of mistaking the entire 3 mL insulin vial as the “dose” for hyperkalemia.

Stock the appropriate syringes. Provide insulin syringes (available in three barrel sizes: 1 mL, 1/2 mL, 0.3 mL) to all patient care units where the drug may be administered, and in any treatment kits that require insulin administration (e.g., hyperkalemia kit). The risk of dosing errors can be reduced if only the smaller barrel insulin syringes are available in units where insulin doses rarely exceed 30 units (0.3 mL barrel) or 50 units (½ mL barrel). Remove tuberculin syringes from patient care areas if they are rarely needed, and dispense a tuberculin syringe only with a product that requires its use.

Label vials and syringes. Vials of insulin dispensed from the pharmacy should be labeled appropriately and include the patient’s name. Tadpole labels (a label with a clear “tail” that wraps around the vial and a “head” on which patient information can be documented) or label flags can be used on smaller 3 mL vials; however, care must be taken not to obscure important product information on the vial. The pharmacy should provide labels for the nurse to complete and affix to insulin vials that are stocked in automated dispensing cabinets (ADC) or refrigerators. These labels should be available in the same cabinet pocket as the insulin vial and should be stocked with the same diligence as the insulin itself to ensure accuracy. Labels that can be completed and affixed to an insulin syringe should also be readily available in all patient care units.

Separate and verify drugs. Do not leave vials of insulin on counters or on top of drug carts. Return them to the appropriate storage location after use. If insulin vials are stored in ADCs, place each type of insulin in a separate pocket or lidded bin to help avoid mix-ups. Use prefilled syringes of heparin for essential central line flushes, and when possible, have pharmacy dispense heparin loading doses. When available, use barcode scanning during product selection when stocking, dispensing, and administering medications. If pharmacy-prepared, barcode-labeled syringes containing patient-continued on page 4 — Insulin
**Special Announcements...**

**Fellowship opportunities**
ISM P is now accepting applications for three 2013-2014 Fellowships. One Fellowship is tailored to a physician resident and includes a local hospital safety rotation. The second Fellowship provides on-site experiences with both ISM P and the US Food and Drug Administration. The third Fellowship provides an opportunity to work on national and regional medication safety projects. For details, visit: www.ismp.org/profdevelopment/.

**ISM P webinars**
Join us for our March 14 webinar, Reducing IV Admixture-Related Safety Risks: Implementation of the ISM P Guidelines for SAFE Preparation of Sterile Compounds. The speakers will focus on serious errors that have occurred with sterile preparations and the implementation of consensus recommendations developed during a national summit hosted by ISM P.

Join us for our April 23 webinar, Safety Strategies with Oral Chemotherapy. The speakers will discuss the safety challenges associated with the growing availability of oral chemotherapy agents, and the implementation of safeguards and best practices for these therapies.

For details on both webinars, please visit: www.ismp.org/educational/webinars.asp.

**Unique 2-day program**
Attend ISM P’s Medication Safety Intensive workshop, an interactive program to sharpen your risk assessment and event investigation skills and learn about Just Culture. The workshop will be held in Tampa, FL, on March 7-8. For details, please visit: www.ismp.org/educational/MSI.

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Specific insulin doses are not provided, it may be necessary to bring the patient’s vial of insulin to the bedside to scan before preparing the patient’s dose.

Don’t assume there will be no problems. When you transition away from using insulin pens, it may be helpful to first conduct a failure mode and effects analysis so you can proactively anticipate and address problems that are sure to arise. During transition, audit health records for episodes of hypoglycemia and hyperglycemia to monitor for system barriers. Encourage staff to report any confusion or hazard. Enhance ongoing surveillance of proper technique for withdrawing and measuring insulin doses. Don’t let your guard down with this high-alert medication.

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Cycles of IV chemotherapy. Tretinoin was to continue on an outpatient basis, along with IV chemotherapy per protocol. But instead of the two 14-day cycles of tretinoin as intended, an oncology clinic nurse enrolled the patient and prescriber in the iPledge program and called in a prescription for CLARAVIS (ISOTretinoin [13-cis retinoic acid]; other brands include AMNESTEEM, MYORISAN, and SOTRET) to a local pharmacy. The clinic nurse did not realize that tretinoin and ISOTretinoin were not the same medication. She was probably more familiar with ISOTretinoin because it is prescribed more frequently than tretinoin in many pediatric oncology centers. The pharmacist at the local pharmacy did not have access to the patient’s clinical information, and the physicians continued to use the abbreviation “ATRA” in their office notes, never noting the generic/brand name of the medication on the patient’s profile. Thus, the patient began to take Claravis at home, not tretinoin.

When the patient was admitted to the hospital again about 4 months later, inpatient chemotherapy orders included tretinoin but requested the use of the patient’s home supply. When an inpatient nurse and pharmacist checked the patient’s supply, they realized it was ISOTretinoin and not tretinoin as intended. The patient’s physicians were contacted and the family was informed of the error. Fortunately, the patient did not experience any reported adverse effects while taking Claravis or lack of disease control while not taking the correct drug. So far the patient continues to be in remission.

ISOTretinoin can be used in chemotherapy treatment protocols in addition to its use in treating severe recalcitrant nodular acne. There is an unlabeled use in children for neuroblastoma at 160 mg/m2/day in two divided doses. Tretinoin is used almost exclusively for APL. The recommended dose is 45 mg/m2/day administered as two evenly divided doses until complete remission is documented. Therapy should be discontinued 30 days after achievement of complete remission or after 90 days of treatment, whichever occurs first. Both tretinoin and ISOTretinoin are available in liquid filled 10 mg capsules, but ISOTretinoin is also available as 20, 30, and 40 mg capsules. ISOTretinoin patients must be enrolled in the iPledge program, but tretinoin does not require enrollment into any registry.

Bottom line, this type of medication error associated with similar medication names is best prevented during the prescribing process with the use of a well-designed order set for APL, highlighting that tretinoin (and not ISOTretinoin) should be prescribed. Referring to the drug as all-trans retinoic acid rather than tretinoin may also help differentiate it from ISOTretinoin; however, use of the acronym ATRA alone is discouraged. This error also highlights the importance of requiring the pharmacist filling this prescription to know the patient’s diagnosis and the drug’s clinical indication at the time the prescription is filled.