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ISMP

Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Hardwiring safety into the computer system

One hospital's actions to provide technology support for U-500 insulin

As the obesity epidemic continues and insulin resistance problems worsen, larger doses of insulin are more frequently required to meet glycemic goals in patients with diabetes. This has led to an increase in the use of U-500 insulin when dose requirements exceed 200 units per day. Given the lack of a U-500 syringe (or pen until very recently), patients and practitioners had been forced to improvise by measuring and communicating doses in "syringe units" if using a U-100 syringe, or by volume markings if using a tuberculin syringe. Confusion regarding the actual dose or proper measurement of U-500 insulin has contributed to a rising number of reported dosing errors, including serious underdoses and overdoses.

To reduce the risk of harmful dosing errors, ISMP has been calling for a U-500 insulin pen since 2013 (www.ismp.org/sc?id=1716). This recommendation was strengthened after a study by the Department of Veterans Affairs found that almost half of clinicians, and even more patients, had selected a U-100 syringe to measure U-500 insulin doses below 100 units instead of a U-500 syringe prototype that was being tested (www.ismp.org/sc?id=257). Participants mistakenly believed the measurement would be more accurate with the U-100 syringe; thus, a U-500 insulin syringe may not prove helpful in preventing dose measurement errors. In December 2015, the US Food and Drug Administration (FDA) approved Eli Lilly and Company's **HUMULIN R U-500 KwikPen** (insulin regular), a 3 mL prefilled pen holding a total of 1,500 units. With the KwikPen, which has been available since last month, dose conversion is no longer needed. The patient's actual dose of U-500 insulin (rounded to the closest 5 unit increment) can be selected by turning the dosing dial.

Now that a U-500 insulin pen is on the market, ISMP recognizes that some hospitals may consider using it for inpatients and outpatients as a way to eliminate dose conversion problems, particularly if the pharmacy staff is unable to dispense each dose in a syringe as prescribed for each patient. We know decisions regarding pen vs. vial use may not be clear-cut for all hospitals.

Whether your hospital is using the U-500 insulin pen or vial, it is vital to ensure safety given the insulin's high concentration. One of ISMP's colleagues, **Steven B. Meisel, PharmD, CPPS**, the Director of Patient Safety at **Fairview Health Services** in Minneapolis, has been working with his organization's information technology staff to do just that and has offered to share the technology enhancements they created in an Epic system that were made to support safe use of U-500 insulin. In Dr. Meisel's health system, the U-500 insulin pen is in use; however, the technology enhancements made in the health system are applicable with minor text adjustments to all hospitals that use U-500 insulin. What follows is a detailed description of the safeguards built into the prescriber order entry system, pharmacy order verification system, nursing medication administration record (MAR), and patient discharge instructions to support safety when prescribing, dispensing, and administering U-500 insulin. Screen shots to help follow

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Reminder: Eliminating ratio expressions. According to USP39-NF34 (The US Pharmacopeia [USP] and The National Formulary [NF]), which became official on May 1, 2016, ratio expressions on single entity drug products are no longer acceptable. Manufacturers should only display **EPI-NEPH**rine 1:1,000 injection as 1 mg/mL, and 1:10,000 must only be displayed as 0.1 mg/mL. The total content per volume in the container will be prominently labeled along with the content per mL. Ratio expressions for neostigmine and isoproterenol are also

Figure 1. Hospira's **EPINEPH**rine ampul label, before (L) and after (R) the change to metric only.

unacceptable. Some manufacturers have been making the change for a while or have already begun conversion (**Figure 1**), but complete inventory turnover will likely take some time. Still, it's not too early to let prescribers know about the changes, and encourage them to begin using only metric dosing. Product labels currently express the strength both ways. Ratio expressions are a known cause of errors (www.ismp.org/sc?id=1718), and continued prescribing in terms of a ratio expression, after product labels no longer mention that, could lead to confusion and calculation errors.

Be sure to educate staff that continue to use ratio expressions. Review order sets, policies, procedures, codes carts, and other emergency kit listings, and all databases that may need to be changed. Drug storage labels should also communicate strengths in metric weights to avoid confusion. The ratio expression for local anesthetics that have more than one ingredient, such as li-

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along with the descriptions of the technology enhancements above can be found at: www.ismp.org/sc?id=1730.

1 Selecting the Order Panel

Prescribers who order Humu**LIN** R U-500 must first select the drug from a pick list, which includes a notation that the drug is a "very high concentration." When the drug is selected, an order panel is presented on the screen, which must be used to prescribe the drug. The three components of the order panel are preselected for implementation by default. Although the prescriber can deactivate these preselected orders, to date, such occurrences are said to be rare. The three preselected orders that accompany the medication include:

Glucose monitoring by nursing at the point-of-care

This order includes routine testing 4 times daily before meals and at bedtime, along with details regarding the testing schedule for the initial 24 hours (e.g., when to start testing, additional testing at 2 a.m. and 5 a.m. during the initial 24 hours).

Pharmacy inpatient consult

This is an order for a one-time consult with a pharmacist who, after consulting with the patient, must add an admission medication history note in the electronic health record using an "RxInsulinConc" phrase (to promote searching for the pharmacy consultation note). The pharmacist should determine if the order for U-500 insulin is a continuation of home therapy, and if the patient has been using a pen or a vial at home. If the vial is used by the patient, the pharmacist should interview the patient to determine exactly how the dose is being measured and prepared, and cross-check that assessment with the patient's ordered dose.

Endocrinology inpatient consult to follow patient during hospitalization

This is a required consultation to endocrinology for glycemic management recommendations and to follow the patient during hospitalization. Directions for contacting the on-call endocrinologist are provided in the order panel. For hospitals in the system that do not have an endocrinologist on staff, separate instructions to consult a clinical nurse specialist for diabetes is also provided.

2 Issuing a Best Practice Advisory

Once the prescriber has selected the U-500 insulin, an *urgent patient care advisory* is always presented on the screen, stating:

> You are placing an order for insulin U-500 (high concentration). The dose should be ordered as **actual insulin units** (NOT markings on the syringe). Please check the patient's dose and consider switching any patients using U-500 insulin in a vial to the PEN at discharge.

The prescriber can either accept the advisory or cancel it to continue the prescribing process.

3 Prescribing the Dose

Prior to entering the dose, the prescriber is reminded via prepopulated order instructions that a very high concentration of insulin (500 units/mL) has been ordered, and that the dose must be prescribed as actual units of insulin, not syringe markings. There is also a reminder that the dose must be ordered in 5 unit increments since the organization only dispenses pens. The order entry sys-

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docaine 1% and **EPINEPH**rine 1:100,000 injections, will retain ratio expressions for the **EPINEPH**rine component because a decimal notation for such a low strength could easily be misread.

Methotrexate-metolazone mix-ups. A *Washington Post* article last week (www.ismp.org/sc?id=1727) detailed a lawsuit that resulted in a $125,000 award (initially $2 million before a judge lowered it) after a patient died from a methotrexate overdose. The drug was dispensed instead of metolazone, which was the prescribed drug. The error began upon discharge when a hospital nurse called in 8 discharge medications to a pharmacy. Unfortunately, one of the oral prescriptions was transcribed incorrectly at the pharmacy as methotrexate 2.5 mg daily instead of metolazone 2.5 mg. During the trial, there was plaintiff testimony that methotrexate is a high-alert medication for which specific precautions should be taken, including segregation of the drug away from the other stock in the pharmacy, mandatory patient counseling, and use of a hard stop in dispensing software to prevent "one tablet daily" instructions on the label.

Also last week, we received a similar error involving methotrexate 2.5 mg dispensed by a pharmacist for an ambulatory care patient instead of the prescribed metolazone 2.5 mg. The prescription was sent electronically to the pharmacy but didn't automatically transfer into the pharmacy computer, so it needed to be transcribed. At that point, methotrexate was selected incorrectly, and then later, a second pharmacist missed the error when she checked the drug by reading the pharmacy label and the product label, but not the image of the original prescription. The patient took methotrexate daily for 1 week until she developed mouth ulcers. She was treated by her physician and is now doing well. We also received reports of mix-ups between metolazone and methadone, both of which can have overlapping tablet strengths and doses, and a report in which metolazone 4 x 2.5 mg tablets to be taken weekly was dispensed instead of the prescribed 4 x 2.5 mg tablets of methotrexate.

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tem automatically rounds the dose to the nearest 5 units if the prescriber has not done so.

4 Prescribing the Route

The route field is prepopulated with the subcutaneous route, which is the only choice available, as U-500 insulin should not be administered intramuscularly or intravenously.

5 Prescribing the Frequency

The order entry system limits the possible frequencies for administering U-500 insulin to those that are appropriate. The most common frequencies are provided as quick-select buttons, and a menu can be accessed to select other appropriate frequencies. This keeps the prescriber from ordering U-500 insulin too frequently. A selection for "user specified" directions is available, but has rarely been used to date.

6 Issuing Alternative Alerts

The prescriber will receive the following alternative alert if he or she attempts to reorder U-500 insulin via a vial from a previous admission or from a "prior to admission" list of medications:

> Please select the alternative order below (Humu**LIN** R U-500 KwikPen 500 Units/mL subcutaneous solution).

Please note: The alternative order takes the prescriber to the U-500 insulin order panel, as this is the only way to order U-500 insulin for a hospital patient.

The prescriber will also receive an alternative alert when entering an ambulatory or discharge order for U-500 insulin via a vial, although the prescriber can proceed with prescribing a vial if desired:

> Consider switching to the U-500 insulin pen (Humu**LIN** R U-500 KwikPen 500 Units/mL subcutaneous solution). There is a patient safety advantage to using the pen, since dosing is in actual insulin units and there is no dose conversion needed.

7 Issuing an Alert During Order Verification

After the pharmacist verifies the prescriber's orders, a best practice alert will appear on the screen if a pharmacist's consulting note has not been entered using the "RxInsulinConc" phrase. The alert reminds the pharmacist to add an admission medication history note using an "RxInsulinConc" phrase, to determine if this is a continuation of home therapy, and to determine if the patient has been using a pen or a vial. If the patient uses a vial at home, the pharmacist is instructed to interview the patient to determine exactly how the dose is being measured and prepared, and to cross-check that assessment with the patient's order(s).

8 Pharmacy Consulting and Documentation

After consultation with the patient, the pharmacist is offered three standard choices from which to choose when documenting the patient's dose at home:

- The insulin was supplied in a U-500 pen. There is no dose conversion with the pen.
- The insulin was supplied in a vial, and measured with an insulin syringe. The patient's actual dose of insulin is [insert appropriate text] units, which the

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In addition to the testimony above, ambulatory care pharmacy staff should never check medicine labels alone against the product container as a final check, without verification of the original prescription or transcription of an oral prescription. Patient counseling offers another opportunity to detect an error. A patient counseling checklist to aid in educating patients is available on our consumer website in English and Spanish (www.ismp.org/sc?id=1709).

Strength confusion. A new cystic fibrosis treatment, **ORKAMBI** (lumacaftor and ivacaftor), is available in a 2-part blister pack, each containing two 200 mg/125 mg tablets (**Figure 1**), for a total of 4 tablets. Listing the strength for just 1 tablet on a 2-tablet blister can be confusing. In one hospital, the first time the drug was prescribed, a pharmacy technician thought that 4 tablets were needed for a 400 mg/250 mg dose. Vertex Pharmaceuticals was contacted and confirmed that *each* tablet is 200 mg/125 mg, so each 2-tablet pack contains 400 mg/250 mg.

We've seen this type of packaging confusion in the past with other drugs (**Figure 2**). The danger is that clinicians, parents, and patients may see "200 mg/125 mg" and think the 2 tablets equal that dose, and then give all 4 tablets in the 2-part packages that are contained in cartons of the drug.

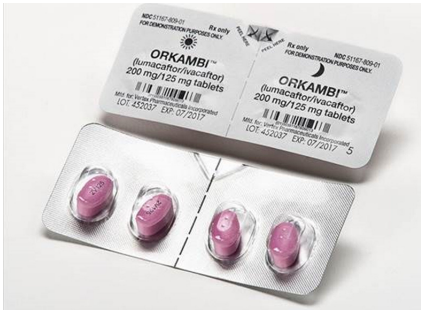

Figure 1. (above) Confusing blister package label for new Orkambi tablets.

Figure 2. (2 photos to left) How much acetaminophen is in this package? There's 325 mg in each tablet. The label was later changed to 650 mg.

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patient measured by drawing the insulin to the [insert appropriate text] unit marking with a U-100 insulin syringe.

- The insulin was supplied in a vial, and measured with a tuberculin syringe. The patient's actual dose of insulin is [insert appropriate text] units, which the patient measured by drawing up [insert appropriate text] mL with a tuberculin syringe.

9 Issuing an MAR Alert

If a nurse selects U-500 insulin for administration within 6 hours of the prior dose, a *critical patient care advisory* appears on the screen stating:

> A U-500 insulin dose was administered in the last 6 hours. U-500 insulin doses should be separated by at least 6 hours in most cases. Please contact the pharmacist for guidance on when this dose should be administered.

The nurse can either accept the advisory or cancel it to continue the administration process.

10 Educating the Patient at Discharge

If the pharmacist has documented that the patient was using a vial of U-500 insulin in the home, but the prescriber has ordered a pen at discharge, the patient will receive a discharge summary (after visit summary) that includes these instructions, which reinforces the verbal education the patient receives:

> **U-500 Insulin Pen:** Our records indicate you have been using U-500 insulin supplied in a vial in the past. Your doctor has now prescribed a U-500 insulin pen. When using the pen, the dose is measured in actual insulin units, which is different from the markings on the syringe you may have been using previously. Before leaving the hospital, make sure you know your insulin dose and understand how to use the pen.

We thank Dr. Meisel for sharing these electronic safeguards and messages associated with certain aspects of using U-500 insulin. We found the details helpful in understanding how the various safeguards and alerts will likely improve safety when using U-500 insulin. We hope other hospitals that use or plan to use U-500 insulin will follow suit and work with their information technology staff and system vendors to make similar adjustments to their medication use systems to help support safety with this concentrated insulin. We look forward to providing readers with an update regarding continued success or future adjustments to these processes once they have been implemented for a longer period of time. Please feel free to send any comments or suggestions to ISMP (ismpinfo@ismp.org), and we will share them as appropriate.

Additional notes

As with any insulin pen, steps should be taken to ensure that the U-500 insulin pen remains "patient specific" and is never shared or used with another patient, even if the needle has been changed. Any insulin pen in use should also be labeled with a distinct patient-specific and drug-specific barcode that is scanned before dispensing and administration to verify the correct insulin type and correct patient. U-500 insulin pens should be dispensed from the pharmacy when prescribed, and neither vials nor pens should be stored in automated dispensing cabinets. For inpatients, dispensing individualized, patient-specific U-500 insulin doses in syringes from the pharmacy may be a safe alternative to the U-500 insulin pen in many hospitals.

Your *Reports* at *Work*

New brand name for vortioxetine. The US Food and Drug Administration (FDA) announced this week that it has approved a brand name change for the antidepressant **BRINTELLIX** (vortioxetine) to **TRINTELLIX**, to decrease the risk of prescribing and dispensing errors resulting from name confusion with the anticoagulant **BRILINTA** (ticagrelor) (www.ismp.org/sc?id=1717).

We first reported a mix-up between these two drugs in our June 19, 2014 newsletter. Brintellix was relatively new on the market (approved in September 2013), and it shared the same first three letters, as well as a few other letters, with Brilinta. Although the 2014 report was the first ISMP received about an actual error, an earlier report had been received from a practitioner who was concerned about the look-alike names. We included a reminder about potential name confusion in our January 29, 2015 newsletter, and on July 30, 2015, the FDA issued a Drug Safety Communication about prescribing errors after reviewing 50 reports of name confusion since Brintellix was approved (www.ismp.org/sc?id=601). In our September 10, 2015 newsletter, we reported additional errors and called for a name change for the newer drug on the market, Brintellix.

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 and administrators should start using the new brand name and NDC number once the company, Takeda, makes vortioxetine available as Trintellix, anticipated in June 2016. "Because of the lag time associated with manufacturing bottles with the new brand name, healthcare professionals and patients may continue to see bottles labeled with the brand name Brintellix during the transition period," FDA warned. Including the purpose with orders and prescriptions for these medications is still recommended.

Fifty hospital employees given insulin instead of influenza vaccine

Our Brazilian sister organization, ISMP Brasil, distributed a national alert last week after being notified of an error at a hospital where 50 employees received a dose of insulin instead of influenza vaccine (www.ismp.org/sc?id=1719). The person in charge of vaccination of hospital staff confused the multiple-dose vials, which were similar in appearance, and she took the wrong box out of a refrigerator where both insulin and influenza vaccine were stored. She administered the wrong substance to her colleagues and to herself. The administration of vaccines began at 9 a.m., and the error was discovered around 10 a.m., at which time glucose injections were administered. All of the employees who received an insulin injection were hospitalized for observation until later in the evening. Although not mentioned, the erroneous insulin dose was likely 50 units or 0.5 mL, the typical influenza vaccine dose.

The exact same error, administering insulin instead of influenza vaccine, has been reported many times around the world, including several cases in the US. Some cases have been fatal. In 1997, The World Health Organization (WHO) reported an incident in which 27 infants died after receiving insulin instead of diphtheria, pertussis, and tetanus (DPT) vaccine (www.ismp.org/sc?id=1720). Errors similar to these mix-ups have also happened with administering influenza vaccine instead of purified protein derivative (PPD) skin tests for tuberculosis, and neuromuscular blockers instead of influenza vaccines, due to non-segregated storage in emergency department refrigerators (www.ismp.org/sc?id=1715).

Keeping influenza vaccine readily available next to other medications can lead to errors. We strongly advise storing vaccines away from other drugs, in a separate refrigerator. The Centers for Disease Control and Prevention (CDC) recommends keeping vaccines in storage units dedicated only to vaccines (www.ismp.org/sc?id=1721). These incidents show how important regular, thorough drug storage checks in hospitals and ambulatory care areas are to observe and address potentially hazardous storage conditions. Errors involving look-alike vials can also be prevented by using commercially available prefilled syringes of vaccines.

Here are some other reports of insulin injections given instead of influenza vaccine:

- October 2014 in St. Louis County, Missouri, 5 teachers received insulin instead of influenza vaccine (www.ismp.org/sc?id=455).
- In January 2010 in Wellesley, Massachusetts, staff at a school received insulin instead of influenza vaccine (www.ismp.org/sc?id=1723).
- In 2007, a teacher in Attleboro, Massachusetts, received insulin instead of influenza vaccine (www.ismp.org/sc?id=1722).
- In November 2009 in Holland, 11 elderly residents in a nursing home received insulin instead of influenza vaccine (www.ismp.org/sc?id=1724). One of the patients later died (www.ismp.org/sc?id=1725).
- In 2008 in Bedford County, Virginia, 5 school employees were hospitalized after a school nurse administered insulin instead of the influenza vaccine (www.ismp.org/sc?id=1726).

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The dose is typically 2 tablets every 12 hours, but patients with severe hepatic impairment or on certain medications should receive 1 tablet every 12 hours. Thus, a patient with hepatic impairment could receive both tablets. Dosing is explained well in the package insert but not on the blister label. The barcode on the label includes the NDC, so the blister will scan as correct if both tablets are given in error. We've asked the US Food and Drug Administration (FDA) to look into this. A draft guidance from FDA, *Guidance for Industry Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (www.ismp.org/sc?id=1733), recommends labeling unit dose blisters as XX mg per tablet/capsule. For Orkambi, the label should clearly state the strength as "each tablet contains 200 mg/125 mg (400 mg/250 mg total)."

Special Announcements

ISMP webinar

Join us on **May 24** for our next webinar, ***Smart Infusion Pump Integration with Hospital Information Technology: Closing the Gap on IV Medication Errors***. Join our speakers as they share their organization's journey to integrate electronic health records with smart pumps and use data from the integration for learning and improvement. For details, visit: www.ismp.org/sc?id=349.

World Congress

The 5th **World Congress of Clinical Safety 2016** will be held on the campus of Harvard University Medical School, Boston, MA, on **September 21-23**. The congress promotes the science and technology of safety and offers a wide range of topics such as patient safety, medication safety, medical device safety, and other related topics. For information, visit: www.ismp.org/sc?id=1731.

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