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ISMP

Acute Care
ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Prescribing errors with levETIRAcetam oral solution

PROBLEM: A 3-month-old baby girl was evaluated in an emergency department (ED) for a cough, congestion, difficulty breathing, and lethargy. A medication history was obtained from the baby's parents to begin the reconciliation process. According to the parents, the baby was receiving 8 mL of **KEPPRA** (lev**ETIRA**cetam) (800 mg of a 100 mg/mL solution) every 12 hours to treat a seizure disorder that had developed after birth. The clinician taking the medication history did not recognize the dose as being excessive for the baby.

It was determined that the baby required admission to treat her respiratory infection. Based on the medication history provided by the parents, the pediatric resident prescribed Keppra in the same dose, 800 mg, with instructions to administer each dose every 12 hours. Although the resident knew the baby's age and weight, he too failed to recognize that the Keppra dose was excessive, and there was no dose alert issued by the computerized prescriber order entry system to warn him.

The hospital pharmacist reviewed the order and noted the excessive dose based on the baby's age and weight. After verifying the dosing recommendations in a pediatric drug reference, the pharmacist contacted the pediatric resident about the excessive dose. The resident asked the baby's parents to bring the bottle of Keppra into the hospital for verification. The baby's mother told the pediatric resident that the prescription bottle did not have a pharmacy label on it, so she did not bring it into the hospital. The pharmacy label had been placed on the outer carton, which she had discarded after removing the bottle of medicine from the carton. The hospital pharmacist then called the community pharmacy to clarify the details of the dispensed medication. It was confirmed with the community pharmacy that a bottle of liquid Keppra 100 mg/mL had been dispensed with directions to "give 8 mL by mouth every 12 hours." Suspecting that the baby had been receiving an overdose of the drug at home, the hospital pharmacist then continued to investigate how the error had happened.

The hospital pharmacist determined that the baby had been admitted to the hospital about 3 weeks earlier. During that hospitalization, the baby had been receiving Keppra 80 mg every 12 hours, a 20 mg/kg/dose for the 4 kg baby. The hospital pharmacy had dispensed the commercially available product (100 mg/mL) in pharmacy-prepared oral syringes containing 0.8 mL (80 mg) of the drug. So during hospitalization, the baby had received the proper dose. However, upon discharge, the physician had electronically prescribed "8 mL" of Keppra twice daily, without listing the intended total dose or concentration. The reason for prescribing the drug by mL only, and in the incorrect volume (8 mL instead of 0.8 mL) is unknown—perhaps simply a mental slip and lapse. Another possibility is that the prescriber actually ordered ".8" mL of the drug, which, without a leading zero, could have been misread as "8" mL if the decimal point was missed. The hospital pharmacy did not have access to the electronic prescription at discharge for verification, and the unit nurses did not notice the error in the discharge summary, which listed all prescribed medications. The community pharmacy used the only commercially available strength of 100 mg/mL to fill the prescription, for which the prescribed 8 mL was equivalent to 800 mg.

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SAFETY briefs

Look-alike levETIRAcetam and valproate sodium vials. Multiple hospitals have contacted us about lev**ETIRA**cetam and valproate sodium vials (both from Fresenius Kabi) being similar in size and color, and having similar anticonvulsant indications (**Figure 1**). Also, the lev**ETIRA**cetam and valproate sodium vials both have the same concentration, 500 mg per 5 mL. Thanks to good

Figure 1. Positioning the two vials in different alignments shows how similar they can look.

label reading practices, all the hazards reported so far were informational—no actual errors have occurred. We've been in touch with Fresenius Kabi and were told the company is in the process of changing one of the vial labels to reduce error potential. For now, you may want to use a different manufacturer's product for one of the drugs or take other steps to reduce the risk of errors.

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Second FDA-ISMP Fellowship opens

We are very pleased to report that FDA has secured funding for a second **FDA-ISMP Safe Medication Management Fellow** for the coming year. A special application process will be used for this new position. Interested applicants should notify us by email (fellowship@ismp.org) as soon as possible. We will then work with them to assure the application materials are submitted. Once the recruitment process is completed, we'll notify the candidate of the starting date for this second position. Further information on the **FDA-ISMP Safe Medication Management Fellowship** is available at: www.ismp.org/sc?id=1704.

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When the community pharmacist received the prescription, he failed to recognize the significant dosing error. He did not verify the actual dose with the discharging physician, despite the volume-only dose of 8 mL, likely because the oral solution was commercially available in a single 100 mg/mL strength, which might have been included on the electronic prescription. It is not known if the retail pharmacist recognized that the prescription was for a 4 kg baby. (The baby's previous prescription for Keppra 80 mg twice daily had been filled at a different pharmacy shortly after her birth.) A dose alert did not appear when the order was verified in the retail pharmacy system, likely because the child's weight or age was not in the pharmacy computer. Thus, the drug was dispensed as 800 mg twice daily, resulting in the baby receiving a 10-fold overdose at home for about 3 weeks prior to presentation in the ED.

Fortunately, the baby did not seem to have any significant clinical adverse effects upon evaluation of the overdose. The child's initial Keppra serum level was supratherapeutic at 63.4 mcg/mL. (According to *Lexi-Lab & Diagnostic Procedures*, toxic levels have not been well established, but most patients display an optimal response to levels between 5 and 45 mcg/mL.) Keppra was held upon hospital admission. A repeat level several days later yielded a value of 7.8 mcg/mL. The baby was eventually discharged after her respiratory infection was resolved. This time, the baby's physician prescribed Keppra 100 mg (1 mL) by mouth twice daily upon discharge for maintenance of seizure control. The baby was seen in a follow-up visit several weeks later and was doing well clinically.

A number of errors reported to ISMP have been caused by practitioners prescribing an oral solution by volume rather than in metric units by weight. For example, in our April 23, 2015 newsletter, we published a series of errors that had occurred with flecainide oral suspension—the dose was prescribed in volume, but the dispensed concentration was different than what the prescribers thought would be used (www.ismp.org/sc?id=1710). One error involved a 9-month-old infant whose parents were told to increase the dose of flecainide to 4 mL, assuming the concentration was 5 mg/mL as in the original prescription. But the parents refilled the prescription at another pharmacy, receiving the drug in a 20 mg/mL concentration. The infant received 80 mg/4 mL, a 4-fold overdose, resulting in wide complex tachycardia and QRS prolongation.

Safe Practice Recommendations: As a result of this error, the hospital has put safeguards in place that will help prevent future medication errors of this type in the pediatric population. These safeguards and other strategies recommended by ISMP are provided below for consideration and implementation in other hospitals to avoid similar errors.

Order doses by weight in metric units. Express single-entity medication doses in metric weight (e.g., mg, mEq, mcg, units), not the volume alone (e.g., mL), even if an oral solution is available in a single strength. (Exceptions are with some combination oral liquid products in a single strength that can be safely expressed in volume alone, or powders that are not dosed by weight.) Including a metric weight dose improves safety because the volume could differ depending on the concentration of the medication.

Include patient's weight in kg (g) on discharge prescriptions. To improve dosing accuracy of weight-based medications in populations at high risk for dosing errors (e.g., patients weighing 50 kg or less), include the weight in kg (g) on discharge prescriptions. If there is no designated field for this information in your electronic prescribing application, include it in the notes/additional information field until vendors provide a designated field for weight. (Community pharmacists may miss information in non-designated, non-required fields with an electronic prescription; thus, vendors should evaluate the need to

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Cup with wrong measurement marking. A 30 mL dosing cup distributed by Essential Medical Supply (model # C1108) has an incorrect marking of 5 mL at the 10 mL gradation. The cup has the correct mL markings for the other gradations, but sequentially, the markings are listed as 2.5 mL, 5 mL, 7.5 mL, and 5 mL (**Figure 1**). As far as we know, these dosing cups have primarily been distributed to outpatient pharmacies, but please be certain you are not using them. Both the pharmacist at the hospital who reported the error and ISMP have contacted the distributor. We also notified the US Food and Drug Administration (FDA), and the Center for Devices and Radiological Health (CDRH) is investigating the issue. ISMP believes that a recall is in order, but it has not yet occurred. Two-fold dosing errors, which could cause serious harm depending on the drug, are inevitable given the incorrectly marked gradation on the cup.

Figure 1. Cup has 5 mL marking where 10 mL marking belongs.

"Floaters" in liquid melatonin. We received a report about floating numbers found in liquid melatonin. Pharmacists preparing doses of Natrol Melatonin 1 mg/4 mL in oral syringes saw what appears to be the number 2 or 5 floating in the filled syringe (**Figure 1**). Apparently, some of the numbers came off the dropper and were floating inside the 60 mL bottle of melatonin and drawn into an oral syringe! The pharmacist contacted the company and FDA, and so did we. The company is aware of the situation and will notify

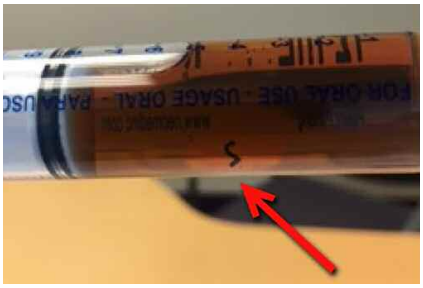

Figure 1. A "floater" is seen in a pharmacy-prepared dose of melatonin.

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include this field for both prescribers and dispensing pharmacists to best safeguard pediatric patients, and even adult patients given the influx of newer, weight-based medications.) Including the patient's weight on prescriptions allows an ambulatory care pharmacist to confirm the ordered dose on the prescription for weight-based medications.

Include the patient's age/date of birth on prescriptions. For appropriate dosing and patient identification, include the patient's age/birthdate on outpatient prescriptions.

Include weight-based and calculated doses. For pediatric medication orders and outpatient prescriptions, include the mg/kg or other dose expression (e.g., mcg/kg) used to calculate the dose, along with the total dose (e.g., 20 mg/kg/dose, 80 mg).

Convert an inpatient order to an outpatient prescription. Require the ordering prescriber to perform the discharge medication reconciliation so that all inpatient and preadmission home medications and doses are reviewed, and if appropriate, converted to outpatient prescriptions. Changes, discontinuations, or the addition of medications upon discharge should be clearly noted in the discharge summary given to the patient.

Verify discharge orders. Require nurses to verify the medications prior to discharge by comparing them with the patient's inpatient medication administration record (MAR) and home medication list. For high-risk patients, such as pediatric patients, also require pharmacists to review all medications listed on discharge summaries, preferably before discharge, but at least within 24 hours of discharge. Like nurses, hospital pharmacists have access to inpatient medication doses to see if there are mismatches with the discharge prescriptions. Report any unexplained discrepancies to the discharging physicians. Be sure to initially and periodically monitor and measure your success with implementing this intervention.

Involve pharmacists in reconciliation. Increase pharmacy involvement in medication reconciliation upon admission to the ED and/or hospital. According to the Agency for Healthcare Research and Quality, the most effective medication reconciliation process involves pharmacists' interventions to clarify doses. Pharmacists, because of their knowledge and skills, are qualified to lead the interdisciplinary effort to maintain an effective medication reconciliation process. Pharmacist involvement is most needed during the initial capture or review of the medications that the patient has been taking at home.

Provide dosing alerts. Enable or build alerts to warn both prescribers and pharmacists about unsafe doses, including weight-based doses, that could cause patient harm. The order entry systems should not allow entry of an order without the patient's age/birthdate and weight populating the requisite, interactive fields to allow the dose warning system to work. Test the alert system periodically, and ensure that the dose alerts are enabled and not bypassed easily without documentation.

Educate patients. Prior to discharge, review each prescribed medication and how to measure each dose with the patient/parents/caregivers. Require the patient/parents/caregivers to demonstrate proper dose measurement of all liquid medications for pediatric patients. (This might have alerted the nurse to the discharge prescribing error, or alerted the parents that an 8 mL dose was a possible mistake.) Remind parents that the measurement device provided at the community pharmacy may be different than that used in the hospital, and to ask the pharmacist if any questions arise about dose measurement. Also remind patients and parents to keep the outer carton of prescription medications if it contains the pharmacy label so they can refer back to the instructions for use. Pharmacists need to do their best to label the container that holds the drug, not the carton alone.

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practitioners once the cause is determined. In the meantime, the organization that reported this issue is utilizing a different liquid product without a dropper.

HIGH-ALERT

Textbook correction. A dose of ibutilide (**CORVERT**) listed in *Demystifying Drug Dosing in Obese Patients* (Shank BR, Zimmerman DE, 2015) was incorrectly stated as 10 mg (one vial) in Chapter 4, page 84, under the heading "ibutilide." The corrected version of the paragraph states that ibutilide is a Vaughan-Williams Class III antiarrhythmic indicated for the rapid conversion of atrial fibrillation or atrial flutter. The dosing for ibutilide recommends a 1 mg infusion IV over 10 minutes for patients who weigh 60 kg or more. A second infusion of 1 mg can be given 10 minutes later if the arrhythmias did not cease. No other data are available for dosing in obese patients, and the above dosing of 1 mg should be used. To obtain a replacement of the print and electronic editions, contact the American Society of Health-System Pharmacists by telephone (866-279-0681) or email (publications@ashp.org).

FREE ISMP Resources

Consumer leaflets in Spanish. We now have Spanish translations of our consumer leaflets for 11 high-alert medications, including insulin analogs, methotrexate, fentaNYL patches, enoxaparin, warfarin, and others. The leaflets provide consumers with important safety tips for taking each medication safely. The leaflets are freely available (www.ismp.org/sc?id=1709) and can be reproduced for distribution to patients.

Nurse AdviseERR. Did you know that your hospital is eligible to receive a complimentary subscription to our *Nurse AdviseERR* publication? The monthly newsletter, designed especially for front-line nurses, is sent by email to a nursing representative at each site who takes responsibility for redistributing it to all nurses in the organization. *Nurse AdviseERR* reaches thousands of US and Canadian hospitals, pro-

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Another *twist* in the ENFit implementation process

We learned last week in a letter from BD that the company has decided to launch a new type of enteral syringe that is not going to be compatible with current oral syringes or the ENFit design that hospitals have been expecting since the system was announced. The new BD syringe will have a male tip, while the ENFit syringe is a reverse gender design (a female tip that attaches to male connectors on ENFit feeding tubes). BD said the company is "working with industry partners to ensure that a complete enteral ecosystem is available," which, we assume, means it is working with feeding tube manufacturers to develop devices with which the new BD enteral syringe can be used.

Both syringes (ENFit and BD) comply with an ISO standard that lays out a new enteral connector dimension but does not specifically comment on gender orientation. The US Food and Drug Administration (FDA) also has no requirement in place for one or the other. Additionally, the ISO standard is voluntary and not enforceable.

The BD letter stated that the reason for designing a new enteral syringe is to avert the risk associated with dosing inaccuracy with the new, reverse gender "female" ENFit enteral syringe option. We reported that issue last year (July 30, 2015 newsletter: www.ismp.org/sc?id=641), after ISMP, along with the American Society of Health-System Pharmacists (ASHP) and The Children's Hospital of Philadelphia, held a summit with manufacturers and FDA to address the problem. This resulted in a new ENFit design for low dose syringes that all manufacturers (except BD) have agreed to use to overcome the dosing inaccuracy issue. The new design has been tested, and dosing accuracy and usability have been demonstrated to ISMP.

We fear that the development of a second (and noncompatible) syringe will bring confusion to health systems and possible inventory disruptions at a time when hospitals have been preparing for a transition to ENFit syringes and feeding tubes. This transition must occur soon in California health systems. A California law requires that, as of July 1, 2016, health systems in the state are not permitted to use enteral devices that connect with unrelated systems (e.g., a Luer). Availability of ENFit syringes is imminent. The BD action is counter to what we had hoped would happen—a single, new enteral system to prevent catheter mix-ups with vascular lines. While either of the new devices will accomplish this, it is also predictable that there will be compatibility problems when patients transfer from one healthcare provider to another, or when they are admitted to a hospital with an existing enteral feeding system different than that used by the hospital.

We have not seen the new BD enteral syringe and do not know when it will be available. However, BD has indicated that the initial launch will focus on the NICU patient group. We have made our position known to BD, and also to the Global Enteral Device Supplier Association (GEDSA), the organization rolling out the ENFit syringes.

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viding nurses with practical advice on how to prevent medication errors. The newsletter is offered **FREE** during 2016 through the generous support of **Baxter Healthcare**, **Novartis Pharmaceuticals**, and **Fresenius Kabi**. Your nursing representative may subscribe by clicking on the following link: www.ismp.org/sc?id=384.

Your *Reports* at *Work*

Label improvement for CutisPharma vancomycin kit. ISMP appreciates the improved labeling that CutisPharma has begun to use for its vancomycin oral solution compounding kit. In the past, the diluent and powder container listed the drug name and strength at the top of both bottles (**Figure 1**), making it difficult to tell these apart. In fact, in our October 22, 2015 issue, we wrote about a nurse who gave only the diluent to her patient, thinking it was liquid vancomycin. It was not easy to tell the diluent container from the drug container without reading the full label with great care, which doesn't happen often enough! But now, CutisPharma has revised the container labels by doing what we suggested last fall: print "Diluent" in large, bold text on the diluent label (**Figure 2**). That's likely to help avoid errors. We thank CutisPharma for making this change. The company told us that it is systematically revising other compounding kit labels, too, including omeprazole and lansoprazole.

Figure 1. Prior labeling allowed confusion between the diluent (R) and the vancomycin powder (L).

Figure 2. New labeling clearly differentiates the diluent (L) from the vancomycin powder (R).

Resources and Services

New Free CE from ISMP

ISMP has four new on-demand webinars that address **smart pump technology integration**, **sterile compounding**, **IV push injection**, and **radiology**. These webinars offer a convenient way to earn CE credit at no cost and learn practical strategies for dealing with current medication safety issues. To access them online, go to: *www.ismp.org/profdevelopment/otherCEOpportunities.asp*.

Don't Miss Out on Workshop

Time is running out for you to join your colleagues at an **ISMP Medication Safety Intensive (MSI) workshop** in 2016 and learn unique ISMP principles and techniques to maximize your organization's medication safety efforts. For more information or to register, go to: *www.ismp.org/educational/msi/default.asp*.

2016 MSI Workshop Dates:

May 5 and 6 – Boston, MA
December 2 and 3 – Las Vegas, NV

Give to Annual Fund

Supporting ISMP's Annual Fund enables lifesaving information about medication errors and adverse events to reach you sooner. Your charitable donation helps ensure that healthcare practitioners can count on ISMP's newsletters, website, and many other tools and resources. To make a contribution, visit: *www.ismp.org/support*.

Just Culture Certification

Attend an ISMP course **May 10-12 in Bellevue, Washington**, that will help healthcare organizations learn and apply the Just Culture model to reduce adverse medication events. Participants will develop expertise in using the 5 Skills and Just Culture Algorithm, and take part in real world simulations that involve specific case examples. The course offers 20 hours of CE for pharmacists and nurses. For more information or to register, go to: *www.ismp.org/Flyers/Just-Culture-201605.aspx*.

Upcoming Webinar

Smart Infusion Pump Integration: Closing the Gap on IV Medication Errors

May 24, 2016 — 1:30-3:00 PM ET

To register, go to: *www.ismp.org/educational/webinars.asp*.

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