Prescribing and dispensing errors with oral solutions

**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 medication reconciliation process. According to the parents, the baby was receiving 8 mL of Keppra (levetiracetam) (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 who reviewed the order noted the excessive dose based on the baby’s age and weight and 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 continued to investigate how the error had happened.

The hospital pharmacist determined that the baby had a prior admission 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 that 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 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**

*Don’t squeeze the Drop-tainer.* Several patients reported to their local pharmacy that they had run out of their latanoprost ophthalmic solution 0.005% early. They were running out of the medication so early that their insurance plans would not pay for refills and therefore were without the medication for several days. The pharmacy staff confirmed that the patients were using the medication in accordance with prescribed instructions and that the prescription’s day supply had been calculated correctly. However, it was noted that the patients were using a latanoprost ophthalmic solution distributed by Sandoz which is supplied in a round DROP-TAINER bottle. This type of bottle requires a different administration technique than the traditional squeeze bottle in which many other ophthalmic products are packaged. When using the round Drop-tainer bottle, the patient must press the bottom of the bottle, rather than squeezing the sides, to deliver a drop of medication. It was determined that...
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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. 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 baby was eventually discharged after her respiratory infection 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 a single-entity oral solution by volume rather than in metric units by weight. For example, in our April 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. 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: Community pharmacies and physician offices should put safeguards in place that will help prevent future medication errors of this type in the pediatric population. Potential safeguards and other strategies recommended by ISMP are provided below for consideration and implementation to avoid similar errors.

Order doses by weight in metric units. On prescriptions, 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 (or g) on 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 (or g) on prescriptions. If there is no designated field for this information in the 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. The current version of the National Council for Prescription Drug Program’s [NCPDP] SCRIPT standard includes parameters for communicating patient weight, so vendors should include this functionality for both prescribers and pharmacists to better safeguard pediatric patients, and even adult patients given continued on page 3—Oral Solutions

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the patients in the cases above were squeezing the sides of the container which will cause variability in dosing.

During our research, we found that there are 2 versions of the Drop-tainer bottle currently on the market—one round and one oval. The round bottle, as mentioned above, requires the user to push the bottom of the bottle to dispense one drop. However, the oval bottle requires the user to squeeze the sides of the bottle to dispense a drop. We suspect that many pharmacists and patients are unaware of the unique administration technique required for use of the round Drop-tainer bottle, like the one containing latanoprost above.

Avoid abbreviations. A long-term care pharmacy received an order for Vitamin D 50,000 units with the directions “1C PO QM.” The patient was to receive one cap.

Figure 1. To dispense one drop of medication, patients must push the bottom of the round Drop-tainer bottle (left) and gently squeeze the sides of the oval Drop-tainer bottle (right).

Unfortunately, the current product labeling and prescribing information does not provide clear instructions for proper use of the “round” Drop-tainer bottle. A separate patient information leaflet that describes the proper use of the Drop-tainer bottles is available from the manufacturer for pharmacists to distribute to patients. These leaflets include instructions for the “round” and the “oval” versions of the Drop-tainer bottle. It is important for pharmacists to identify the ophthalmic products dispensed in Drop-tainer bottles, particularly the round versions, and ensure patients are educated on the proper administration technique. Hopefully in the near future, clear instructions for proper use will be included in the product labeling.
the influx of newer, weight-based medications. Including the patient’s weight on prescriptions allows a 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 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).

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. Test the alert system periodically, and ensure that the dose alerts are enabled and not bypassed easily without documentation.

Educate patients. Review each prescribed medication and how to measure each dose with the patient/parent/caregiver. Require the patient/parent/caregiver to demonstrate proper dose measurement of all liquid medications for pediatric patients. Ask if the patient has previously taken the medication and at what dose. Remind parents 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.

**Your Reports at Work**

**New brand name for vortioxetine.** The US Food and Drug Administration (FDA) announced earlier this month 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 2014 newsletter. Brinellix 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 February 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 Brinellix was approved [www.ismp.org/sc?id=601]. In our August 2015 newsletter, we reported additional errors and called for a name change for the newer drug on the market, Brinellix.

Pharmacy staff who order and stock the medication should be aware that Brinellix 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 Brinellix, 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 Brinellix during the transition period,” FDA warned. Including the purpose with prescriptions for these medications is still recommended.

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sure by mouth each month. However, the pharmacy inadvertently dispensed Vitamin D 50,000 units with directions to take a capsule daily. The error was caught by personnel in the long-term care facility prior to reaching the patient. In this case, a mix-up between monthly and daily occurred; however, it is also possible that the abbreviation “QM” could be interpreted as “every Monday.” In this day and age of electronic prescribing, it is hard to believe that transmission of directions that include error-prone abbreviations is still possible. Transmission of clear, full-text directions should be the default in electronic systems. Of course, healthcare practitioners should stop using abbreviations such as “OD” and “QM” in all forms of communication. Instead, use the word “daily” and “monthly.”

**Tacrolimus – tamsulosin mix-ups.** Beware of the potential for mix-ups between tamsulosin, an alpha₁ blocker used to treat benign prostatic hyperplasia, and the immunosuppressant tacrolimus. Recently it was discovered that a pharmacy inadvertently dispensed tamsulosin instead of tacrolimus. The omission of tacrolimus places the patient at high risk of organ rejection post-transplant. Including the purpose of the medication on the prescription and opening the bag at the point-of-sale can help catch this type of mix-up.
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 January 2016 and April 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/How_To_Use_AA.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

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<tr>
<td>01/16</td>
<td>U-500 regular insulin pen (HUMULIN R U-500 KWIKPEN)</td>
<td>No dedicated syringe is available to measure doses of U-500 insulin from a vial. Patients and clinicians administering U-500 insulin must use a U-100 syringe or a tuberculin (TB) syringe, both of which risk confusion and serious errors when measuring doses. If using a U-100 syringe, the dose must be converted to the markings of a U-100 syringe, or if using a TB syringe, to the volume markings. Miscommunication of the actual insulin dose based on U-100 syringe markings or volume has also led to serious errors.</td>
<td>The US Food and Drug Administration (FDA) has approved Humulin R U-500 KwikPen, a prefilled pen device. The pen holds 1,500 units, and the dose can be set in 5 unit increments. Consider using the U-500 pen, which is now available, to eliminate dose conversion problems. However, patients using U-500 insulin from a vial may still communicate their dose in U-100 syringe markings or volume, so always verify the dose and syringe/device used at home.</td>
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<td>02/16</td>
<td>Paregoric, not “opium tincture”</td>
<td>Paregoric was recently reintroduced into the market after being unavailable for several years. However, the nomenclature “opium tincture, 2%” was mistakenly added by the manufacturer to the label along with “paregoric.” Paregoric is NOT “opium tincture.” A dose of 5 mL of paregoric delivers 2 mg of morphine; a dose of 5 mL of opium tincture (10 mg/mL) delivers 50 mg of morphine.</td>
<td>The manufacturer is in the process of relabeling this product as paregoric 2 mg/5 mL (0.4 mg/mL). For now, add labels to the bottles so they are not confused with opium tincture.</td>
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<td>04/16</td>
<td>Ask about safety caps</td>
<td>Medication bottles with safety caps are designed to protect children from accidental ingestion, but, on occasion, can contribute to patient harm. An elderly patient with multiple myeloma suffered a spiral fracture of the humerus while trying to remove the child-resistant cap on her medication bottle. The act of pushing down and twisting broke the weakened bone and caused the fracture.</td>
<td>Pharmacists should talk to patients to discuss problems they may have accessing their medications. If patients express difficulty, offer them the choice of having their prescriptions(s) dispensed in a bottle without a safety cap. Make sure to periodically update this type of information. Educate patients about the risk of accidental poisoning of children and safe medication storage (<a href="http://www.upandaway.org">www.upandaway.org</a>).</td>
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<td>Menveo is supplied in two vials, one containing lyophilized powder and the other a liquid component, which must be mixed together prior to injection. A government analysis identified 390 reports involving more than 400 patients during the past 5 years where only one component of the vaccine was administered, usually the MenCYW-135 liquid component. Several patients received only the MenA lyophilized component, reconstituted with a “generic” diluent. Errors are serious because they leave people exposed to a potentially deadly disease.</td>
<td>To prevent these errors, more is needed than just staff education and carefully following instructions—the only strategies suggested in the government analysis. Manufacturers must improve the labeling and packaging of 2-component vaccines to distinguish each container and connect the two so their contents are administered together. Until then, keep two-component vaccines together if storage requirements do not differ. Clearly distinguish each component if the manufacturer’s label could mislead staff into believing either is the vaccine itself. Require barcode scanning of both components prior to mixing and administration.</td>
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**Confusion among “Depo-” medications leads to wrong drug, route, or strength/volume errors**

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<td>03/16</td>
<td>Several drugs are available with names that begin with the prefix “Depo-.” Misadministration of these drugs by the IV route and confusing one Depo- medication with another has been reported frequently. Recently, DEPO-PROVERA (medroxyPROGESTERone acetate) and DEPO-MEDROL (methyl-PREDNISolone acetate) were mixed up; Depo-Medrol was administered IV instead of IM; and the volume/strength of DEPO-TESTOSTERONE (testosterone cypionate) vials was confused.</td>
<td>Recommendations to prevent potentially harmful mix-ups include: utilizing barcode scanning prior to stocking and administering these medications; limiting inventory to a single strength and vial size of Depo-Testosterone; utilizing auxiliary labels to indicate the route of administration; purchasing products in prefilled syringes to differentiate look-alike products; and utilizing tall man letters when expressing drug names. See the FDA and ISMP List of Recommended Tall Man Letters at: <a href="http://www.ismp.org/Tools/tallmanletters.pdf">www.ismp.org/Tools/tallmanletters.pdf</a>.</td>
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**Label characteristics of stock bottles contribute to errors**

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<td>01/16</td>
<td>Various strengths of Apotex’s ARIPiprazole are packaged in bottles of similar size, shape, color, and labeling. Of most concern is that the tablet strengths are displayed at the far right of the label and can be missed if the container is turned slightly. In addition, the strength font size is much smaller than the drug name font size. As a result, a pharmacist picked up the wrong bottle and nearly dispensed the wrong strength of ARIPiprazole tablets.</td>
<td>When there’s a choice of brands for specific products, avoid labels that separate the dose/strength from the product name. Use DailyMed (<a href="https://dailymed.nlm.nih.gov/dailymed/">https://dailymed.nlm.nih.gov/dailymed/</a>) to check container label appearance. Use barcode scanning when selecting products. Call attention to the strength by drawing an arrow from the drug name pointing to the strength. Face labels forward when bottles are stored on a shelf.</td>
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### Issue

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<td>03/16</td>
<td>A nurse transcribed an order for insulin aspart with the frequency as “c B-L-D.” The pharmacist initially misread this as “BID” but upon further review noticed the hyphens between the letters and requested clarification. The abbreviation was intended to mean with breakfast, lunch, and dinner.</td>
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<td>04/16</td>
<td>The US Food and Drug Administration (FDA) announced that it is revising warnings for the use of metFORMIN in certain patients with reduced kidney function. FDA will be requiring manufacturers to change the recommended measure of kidney function used to determine if metFORMIN therapy is appropriate for a patient. The measure will change from one based on a single blood creatinine concentration to one that estimates renal function.</td>
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<td>03/16</td>
<td>The green warfarin 2.5 mg tablet manufactured by Exelan pharmaceuticals looks similar to the blue warfarin 4 mg tablet. This could contribute to dispensing errors as healthcare professionals and patients have become accustomed to standard colors for the strengths of warfarin tablets.</td>
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### Recommendation

Do not abbreviate instructions in handwritten or electronic prescriptions. Avoid ambiguous abbreviations when communicating drug and patient information. Clarify any ambiguity with the prescriber or nurse.

Review the full FDA Drug Safety Communication ([www.ismp.org/se?id=1712](http://www.ismp.org/se?id=1712)), including details on how and when kidney function should be measured in patients receiving metFORMIN. Review with patients the Medication Guide or Patient Package Insert they receive with their prescriptions for metFORMIN-containing drugs.

Determine if your pharmacy stocks the Exelan warfarin product. Inform staff of the possible confusion. Ensure you provide patient education, including opening the prescription bag and bottle with the patient, to answer any questions and increase the chances of intercepting an error.

The keys to success of RCA are the quality of the information collected, careful analysis of the information, and subsequent actions taken to improve the system and prevent harm. ISMP’s [Root Cause Analysis Workbook for Community/ Ambulatory Pharmacy](http://www.ismp.org/tools/rca/) provides community pharmacies with tools designed to meet regulatory requirements in the full investigation of the causes of a sentinel event, and to help identify and implement effective strategies to prevent similar occurrences.

### Date Completed