“Use as directed” can cause confusion for both patients and practitioners

**Problem:** If you are a pharmacist working in an outpatient setting, you have likely received a prescription in which the prescriber used the all-too-familiar sigs “use as directed” (UAD), “take as directed” (TUD), “as directed” (UD), or even the Latin “ut dictum” or “ut dict.” These sigs are ambiguous and do not provide adequate dosing instructions for patients to follow or for pharmacists to counsel the patient. They also make it difficult for hospital practitioners to know how the prescriber intended the medication to be used by the patient and to effectively conduct medication reconciliation or educate patients about drug therapy at discharge. “As directed” instructions invite misunderstandings about the dosing instructions, which have resulted in serious medication errors.

Although these sigs are archaic, some practitioners may believe the “as directed” phrases are only a problem if the directions for the medication can be variable or if the prescribed dose or frequency of use is outside recommended dosing parameters. However, pharmacists cannot assume that the prescriber has educated the patient about how to properly take the medication or that the patient will remember the instructions if provided. Explicit directions including the strength, dose, frequency of administration, route of administration, and duration of therapy (if appropriate) are needed in order for pharmacists to effectively educate patients and for patients to take their medications correctly. Furthermore, certain elements of a prescription (e.g., route, frequency, dosage form) may help pharmacists differentiate between two drug names that look or sound similar.

Several events reported to the ISMP National Medication Errors Reporting Program (ISMP MERP) illustrate errors that have occurred, at least in part, due to a prescription with some form of the “use as directed” phrase as the only dosing instructions provided. Some of these events involved high-alert medications, resulting in serious or potentially serious adverse outcomes for patients.

**Case examples**

**Case #1.** An elderly man experienced a severe hypoglycemic event requiring hospitalization after the man’s son administered 100 units of **NovoLog** (insulin aspart) to his father. The insulin vial was labeled with the following directions: “Insulin aspart 100 units/mL. Give three times a day before meals as directed.” The son, who was the primary caretaker, had not been educated about insulin dosing when his father was discharged from a nursing facility the day before the event. He believed the 100 units/mL strength on the pharmacy label was the dose, given the lack of clarity with the “as directed” instructions.

**Case #2.** A mix-up occurred between **ClinDesse** (clindamycin vaginal cream), used to treat bacterial vaginosis, and **ClinDets** (clindamycin pledges), used to treat acne. A prescriber left a message on a pharmacy’s voicemail system for a prescription for ClinDesse, with instructions to “use as directed.” Upon playback, the order sounded like ClinDets and was processed and dispensed as such. The error was discovered when the patient called the pharmacy to ask how to use the pledgets vaginally.

Continued on page 2—"As directed" >

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Case #3. Three errors involved mix-ups between the intended colonoscopy preparation drug VISICOL (sodium phosphate dibasic and sodium phosphate monobasic) and the opioid VICODIN (HYDROcodone and acetaminophen). In all three instances the prescription for Viscol was provided with “take as directed” instructions. Two of the errors resulted in severe harm after the patients took more than one-dose Vicodin tablets over the course of a single day. (Note: The brand name product Viscol is no longer available.)

Case #4. An electronic prescription for EPIZEP (EPINEPHrine) was accidently transmitted to the pharmacy instead of the intended insulin pen needles. The EpiPen was dispensed to the patient’s wife with the instructions to “use as directed.” The pharmacist assumed that an EpiPen had been previously dispensed to the patient and did not provide counseling regarding its proper use. After experiencing difficulty while trying to connect the EpiPen to the insulin pen, the patient’s wife called the pharmacy and the error was discovered.

Impact of “as directed” on inpatient care

Medication reconciliation. While the prescription sig “as directed” is most often seen with outpatient prescriptions, its use for dosing instructions can lead to medication errors during hospitalization related to medication reconciliation. The medication reconciliation process upon admission can be challenging under the best of circumstances. But if prescription labels on home medications include only “as directed” for the instructions, inpatient practitioners are faced with ambiguous, error-prone dosing information and must undertake the burdensome task of obtaining accurate information from the originating prescriber. Home medication lists that include “as directed” for the instructions do not provide the information necessary for accurate admission prescribing. The patient’s or caregiver’s account of how the medication was being used at home also may be inaccurate.

Discharge education. Prescriptions provided to patients at discharge with instructions to take “as directed” provide no guidance for discharge education. As with the outpatient pharmacist, the hospital nurse or pharmacist may not know if or how the prescriber instructed the patient to take the medication. While patients may be asked to repeat the prescriber’s directions for use, leaving it up to the patient to remember what the prescriber said is not an acceptable solution. In fact, the “use as directed” instructions may discourage redundant education if practitioners are concerned about confusion they may cause by providing directions that differ with what the patient has been told.

Frequency of “as directed” prescriptions

Survey. To learn more about the frequency and use of “as directed” instructions on prescriptions, ISMP conducted an online survey of outpatient pharmacists between May 19 and June 19, 2016. The survey was promoted in both our Community/Ambulatory Care and Acute Care editions of the ISMP Medication Safety Alert! It included 6 questions, 2 of which were related to respondent demographics, and the remaining 4 questions were related to the prevalence of the sig “use as directed” on prescriptions, medications commonly prescribed with “use as directed” instructions, how these prescriptions are sent to the pharmacy, and how pharmacists address these prescriptions.

Results. Despite the wide uptake of electronic prescribing and insurance repayment penalties for discrepancies over the correct days’ supply (which cannot be verified with the instructions “use as directed”), the results of the survey indicate that many drugs are still prescribed and dispensed with the directions “use as directed.” A total of 434 participants responded to the survey, 92.4% of which indicated their country of practice is the US. More than half of participants (55.7%) said that 1 to 5% of all prescriptions they receive are written with a sig of “use as directed.” Less than 10% of participants indicated that they continued on page 3—“As directed” —cont’d from page 1

> SAFETY briefs cont’d from page 1

This is not a new problem. As far back as our August 8, 2001 newsletter issue, we included a hazard warning (www.ismp.org/sc?id=2790) about the two concentrations of the NIMBEX brand of cisatracurium being mixed up. Mix-ups of the two concentrations of both generic cisatracurium and the brand NIMBEX have occurred.

Storage practices may sometimes create a vulnerability that could lead to selection of the wrong product strength. In one of the hospitals where a mix-up took place, both concentrations were stored in the same bin. The pharmacy now separates the two concentrations and labels the 10 mg/mL (200 mg/20 mL) bin, “NOTE—HIGH CONCENTRATION. For pharmacy compounding use only” (Figure 2). The lower concentration bin is labeled

Figure 2. A pharmacy’s storage bin for 10 mg/mL (200 mg/20 mL) cisatracurium.

“2 mg/mL.” Another consideration is to only stock the concentrated product in the IV room in the pharmacy and keep the lower concentration product intended for use in the OR in a separate location. It might also be helpful to draw attention to the products’ strengths by circling the concentration on the carton labels. Also, all refrigerated and nonrefrigerated neuromuscular blocking agents should be segregated from other medications and sequestered in a rapid sequence intubation (RSI) kit or lidded box, pocket, or drawer wherever they are stored in the OR.

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never receive prescriptions written with instructions to “use as directed.” Respondents reported that they receive prescriptions that include the *sig* “use as directed” electronically (84.4%), as handwritten prescriptions (74.6%), and as facsimile prescriptions (55.6%).

Respondents indicated that they most frequently verify the directions with the prescriber (74.7%) when they receive prescriptions written as “use as directed.” However, many also noted that they provide the usual and customary directions for the medication if they exist (59.3%), or they simply place “use as directed” on the bottle (43%). Many respondents noted that they confirm the days’ supply or maximum daily dose with the prescriber for billing purposes. Respondents also identified medications for which they have received prescriptions with the directions “use as directed” (Table 1). “Other medications” not specified in the table include: colonoscopy/bowel preparations, diabetic testing supplies, ophthalmic products, and inhalers.

**Table 1. Medications prescribed with directions of “use as directed.”**

<table>
<thead>
<tr>
<th>Medication/Medication Class Name</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prepackaged items with specific directions for use on the package</td>
<td>75.6</td>
</tr>
<tr>
<td>(e.g., ZITHROMAX Z-PAK [azithromycin])</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>58.4</td>
</tr>
<tr>
<td>Topical medications (standard quantities)</td>
<td>56.1</td>
</tr>
<tr>
<td>Prednisone</td>
<td>55.5</td>
</tr>
<tr>
<td>As needed emergency medications (e.g., EpiPen [EPINEPHRINE], DIASTAT [diazepam], nitroglycerin)</td>
<td>55.0</td>
</tr>
<tr>
<td>Contraceptives (oral)</td>
<td>54.7</td>
</tr>
<tr>
<td>One-time treatments (e.g., for lice or scabies)</td>
<td>54.7</td>
</tr>
<tr>
<td>Insulin</td>
<td>43.1</td>
</tr>
<tr>
<td>Migraine medications</td>
<td>39.9</td>
</tr>
<tr>
<td>Erectile dysfunction medications</td>
<td>33.7</td>
</tr>
<tr>
<td>Injectable to be administered at a clinic (e.g., MYOBLOC [rimobutulinumtoxinB], GARDASIL [human papillomavirus vaccine], ZOSTAVAX [roster vaccine])</td>
<td>26.4</td>
</tr>
<tr>
<td>Fertility injections</td>
<td>11.3</td>
</tr>
<tr>
<td>Hemophilia injections</td>
<td>2.8</td>
</tr>
<tr>
<td>Other medications</td>
<td>19.6</td>
</tr>
</tbody>
</table>

**SAFETY Briefs** cont’d from page 2

Correction to table of patches not safe with MRI. In our August 11, 2016 newsletter article, *Burns during MRI from patches with metal in the backing*, we noted that the Apotex brand of the fen-taNYL patch is not MRI safe. However, Aveva, which manufactures the drug for Apotex, was the manufacturer mentioned in the table. Also, transdermal EXELON (rivastigmine), manufactured by Novartis, was in the table but it does not contain a metal backing, although the generic rivastigmine patch made by Alvogen does have an aluminum-backed and is listed correctly in the table. **NICODERM CO OPAQUE** contains an aluminum-backed, but **NICODERM CO CLEAR** does not. These two products share the same National Drug Code (NDC) number; thus both were thought to contain metal in error. The 21 mg/day strength has both configurations: Opaque and Clear. The 7 mg/day and 14 mg/day forms are now only manufactured in Clear. We are sorry for any confusion. A revised newsletter with the corrected table is available online at: www.ismp.org/sc?id=2791.

Drug database errata. Wolters Kluwer has issued a correction notice for the methylPREDNISolone acetate injection monograph in the *Drug Facts & Comparisons* database available online, and in the 2015 and 2016 editions of the print publication, *Drug Facts and Comparisons*. Information about off-label use and dosing of methylPREDNISolone acetate injection for chronic obstructive pulmonary disease (acute exacerbation) has been removed from the *Drug Facts & Comparisons* database and *Facts & Comparisons* eAnswers but can still be found in the 2015 and 2016 bound versions of *Drug Facts and Comparisons*. For the notice about the revision issued by the company, please see: www.wolterskluwercdi.com/clinical-notices/revisions/.

**Safe Practice Recommendations:** To better safeguard the correct and appropriate use of medications, ISMP and the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) ([www.ismp.org/sc?id=1778](http://www.ismp.org/sc?id=1778)) recommend that prescribers always include explicit directions for use on prescriptions. While prescribers should also instruct patients about the use of any medications they prescribe, specifying the instructions on the prescription reinforces the intended care plan and allows the pharmacist and other healthcare providers, including those providing discharge education, to review the same instructions with the patient. Clear and complete instructions on prescriptions and prescription drug labels are also important to support accurate medication reconciliation during hospitalization.

If a prescription includes the *sig* “use as directed,” the outpatient pharmacist should clarify the directions for use with the prescriber and include those directions on the pharmacy label. For prepackaged items with directions on the package (e.g., Zithromax Z-Pak), some pharmacies use a *sig* code to print the standard directions on the label. If the directions exceed space limitations, a supplemental or overflow label may be required. When changes in the directions for use with medications such as insulin or warfarin have been communicated to the patient by the prescriber, there is an opportunity for the pharmacist’s involvement. When the initial prescription is filled for any medication that often involves frequent dose changes, pharmacists should encourage patients to notify the pharmacy of any dose changes they may receive from the prescriber’s office and discuss with the pharmacist how the leftover dosage form and strength can be used to fulfill the new dosing instructions until a new prescription is necessary. For drug doses that are based on home point-of-care testing, such as prandial insulin doses that may change with each meal, the directions for how to adjust the dose must be clear and explicit.
Dnt abbv drg nms

In a 2014 survey by the American Society of Health-System Pharmacists (ASHP), 94.1% of pharmacy directors reported that their hospitals have implemented an electronic health record (EHR) system, and 80.9% are using computerized prescriber order entry (CPOE) systems. As we’ve seen previously, while health information technologies (HIT) have solved some issues contributing to medication errors such as illegible handwriting, they have introduced risks related to the way drug names and doses are displayed in the computer system. Oftentimes there are space limitations in drug name and dose fields, and this is especially problematic with combination products.

We’ve received two reports about the way EHRs display GENVOYA (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) and STRIKINGLY (elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate). Both medications are manufactured by Gilead and contain 4 drugs in one tablet, given once daily to treat human immunodeficiency virus-type 1 (HIV-1) infection. However, they are not interchangeable. The difference between the two resides with the ester derivative of tenofovir. Genvoxa, which contains tenofovir alafenamide, was approved in 2015. It contains less than one-tenth of the amount of tenofovir found in Strikingly, which contains tenofovir disoproxil fumarate, decreasing the risk of renal and bone toxicity. Unfortunately, computer systems may truncate the medication names, which could lead to errors. In one of the error reports we received, a patient was taking Genvoxa prior to admission. The computer system listed the drug using abbreviated generic drug names and not the brand name. It was listed as “Elviteg-Cobic-Emtricit-TenoAF.” When the pharmacy received the order, Strikingly was mistakenly dispensed for the patient. The patient received one dose of Strikingly before the error was discovered. Fortunately, the patient was not harmed.

To address errors that are specific to HIT, ISMP is currently updating its draft Guidelines for the Safe Communication of Electronic Medication Information based on public comments received from the field. In the meantime, to prevent these specific mix-ups, display both the brand and generic names of the drug when possible and do not abbreviate the drug names. Including the brand name provides clarification and reduces the risk of selecting the wrong drug during order entry or drug dispensing.

References

ISMPSwan webinar
Join us on September 29 for our next webinar, Just Culture: Application of an Accountability Model with Medication Safety Events. This program will explore the basic tenets of a Just Culture and how these tenets can be applied to the investigation of medication safety events and accountability for safety—both system and individual. The speaker will contrast our current culture with a Just Culture, describe how to manage human error, at-risk behavior, and reckless behavior, and provide an overview of the questions and processes most critical to investigation of adverse events. To register, visit: www.ismp.org/sc?id=349.

ISMPSwan MSI
Join us at the ISMP Medication Safety Intensive (MSI) workshop in Las Vegas on December 2 and 3 to learn unique ISMP principles and techniques that can maximize your organization’s medication safety efforts. This workshop will help you learn to identify, analyze, and control medication safety risks using real-world case examples for practice. For more information or to register, visit: www.ismp.org/sc?id=351.

Put your boots on...

ISMP will be holding its 19th Annual Cheers Awards dinner on Tuesday evening, December 8, at Stoney’s Rockin’ Country in Las Vegas! Each year, ISMP celebrates individuals and organizations that have set a standard of excellence in the prevention of medication errors during the previous 12 months. Nominations for this year’s Cheers Awards are still being accepted through September 9. ISMP accepts outside nominations, including self-nominations. To submit a nomination, please visit: www.ismp.org/sc?id=1777. To join us at the Cheers Awards dinner, please visit: www.ismp.org/Cheers/dinnerReg.asp. We hope to see you there!