Drug Labeling and Packaging — Looking Beyond What Meets the Eye

Ambiguous and confusing packaging and labeling as well as look-alike or sound-alike drug names significantly contribute to medication errors. In fact, a frequent (29%) cause of pharmacy drug dispensing errors is failure to accurately identify drugs, usually due to look-alike or sound-alike drug names.1

Errors may occur when important information is printed in an inconspicuous place on the label, presented in an ambiguous manner, or overshadowed by less important information. The printing on the label may also be less than optimal in size, boldness, or contrast. Ornate graphics, emphasized corporate names, or logos may distract from the primary purpose of the label: to permit the user (i.e., pharmacist, nurse, physician, patient) to identify the name(s), dosage form, and strength of the product. Complicating the situation is that healthcare practitioners often read labels under less-than-ideal conditions (e.g., in a patient's room at night when lights are dimmed, during emergency situations).

Confirmation bias also plays a role in product mix-ups.2 Errors are often induced by familiarity with procedures and materials, coupled with the tendency for people to see what is familiar or what they want to see, rather than what is actually there. Recent healthcare graduates, not yet familiar with many medications, initially will read labels carefully. After a while, they may rely on the appearance of a familiar product and become less vigilant when reading labels. If a drug has distinctive packaging, the potential for mix-ups may be reduced. If several products have similar packaging or if labeling is hard to read, the potential for error involving confirmation bias increases.

There are many factors related to a medication’s label or package design that can contribute to errors. This article will focus on some of these factors as seen in PA-PSRS data, including the following issues:

- Readability of labels and packaging
- Expression of the drug’s strength or concentration
- Use of color
- Lack of contrast

Readability of Labels and Packaging

Many words or images that routinely appear on medication labels serve to meet regulatory requirements more than the end users' needs. For example, the wording that appears on bags of infusion solutions (i.e., solutions commonly used to provide hydration) is cluttered with irrelevant information, causing further confusion to the practitioners using the product. (See Figure 1.)

Mix-ups between similar solutions are common in the PA-PSRS database. In fact, 8.7% (almost 1,400 reports) of wrong-drug and wrong-concentration errors involve mix-ups between these solutions.

Figure 1. Similar Labeling of Hydration Solutions has Led to Many Errors Reported to PA-PSRS. (Liter bags of Dextrose 5% and Sodium Chloride 0.45% with Potassium Chloride 20 mEq on the left and Sodium Chloride 0.9% with Potassium Chloride 20 mEq on the right.) Image provided courtesy of ISMP.
Expression of the Drug’s Strength or Concentration

The way a manufacturer presents the strength or concentration of a drug can be confusing and may lead to errors. For example, there have been reports to PA-PSRS and other reporting programs in which the label on a multidose vial expressed the concentration as the amount of active drug per 1 mL (e.g., 1 mg/mL), yet the vial contained more than 1 mL of solution (e.g., 5 mL) and did not indicate the total amount of drug in the vial (e.g., 5 mg/5 mL). The following report submitted to PA-PSRS mentioned an event that occurred due to similar circumstances.

Doctor took Kenalog 40 mg/5 mL vial out of Pyxis machine. After the doctor injected the patient’s shoulder, he realized that the concentration was 40 mg/mL, and the whole vial (5 mL) was given.

The carton and vial labels of each of these products prominently display 40 mg. But the multidose vial only displays the concentration as a 40 mg/mL rather than 200 mg/5 mL (see Figure 2). The facility indicated that staff will now store the vials (5 mL and 1 mL) in separate areas in the pharmacy, only the 40 mg/1 mL concentration will be stocked in their Pyxis machine, and bar-code technology will be used to scan all medications prior to stocking the Pyxis machines.

Another report submitted to PA-PSRS mentions an event that occurred with a 20 mL vial of gentamicin that was labeled as 40 mg/mL.

The certified registered nurse anesthetist (CRNA) read the gentamicin vial as 40 mg per 1 mL but gave the entire vial (20 mL or 800 mg). The multidose vial was new to the operating room. When the CRNA became aware of the error, the surgeon was notified immediately. The patient was hydrated to dilute the medication.

This organization permanently removed the multidose vial from the operating room.

In another case reported to the Institute for Safe Medication Practices (ISMP), an order from the emergency department (ED) was received in the pharmacy for “ZEMURON (rocuronium) 40 mg IV now.” A pharmacy technician removed a carton of the drug from the refrigerator to verify what she was entering into the computer. Upon seeing 10 mg/mL prominently displayed on the box (see Figure 3) and the vial, the tech entered an order for 4 vials, believing all were needed for a 40 mg dose. Actually, the vials contained 10 mL with a total of 100 mg per vial. The tech showed the order, label, and four vials to the pharmacist, who also misinterpreted the total dose in each vial and approved delivery to the ED. The total volume in each vial was probably missed because this information does not appear within the box that lists the concentration. Fortunately, the ED nurse recognized the mistake before administering the drug.3

ISMP believes product labels should prominently display the total contents. Both the total volume and amount in metric weight (e.g., 10 mg/5 mL) and the concentration per milliliter (e.g., 2 mg/mL) should appear side-by-side or one just above the other, within the same border or shaded background, even on multidose vials.4

The expression of drug concentrations on package labeling as a percentage or ratio of weight to volume...
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is problematic. For most injectable products, the concentration is expressed in milligrams or micrograms per milliliter (e.g., mg/mL), but the concentration of a few drugs is expressed as a dilution ratio or percentage (e.g., epinephrine 1:1,000, lidocaine 1%). Studies show that prescribers’ knowledge about concentrations expressed as a ratio or percentage is inadequate, even among physicians and emergency medicine residents. These expressions are commonly used for drugs in resuscitation (e.g., epinephrine, lidocaine, neostigmine, sodium bicarbonate). A wrong dose or life-threatening delay in treatment is possible if these drugs are prescribed in milligrams (which requires knowledge of ratio or percent concentrations and calculations) or milliliters (a problem if multiple concentrations exist). Many reports have been submitted to PA-PSRS and other reporting programs in which undiluted epinephrine 1:1,000 (1 mg/mL) was given intravenously (IV) instead of 1:10,000 (0.1 mg/mL) concentration. In some of these cases, practitioners did not understand the ratio expression and accidentally prescribed or administered the wrong medications.

The labeling of oral solid dosage forms in unit dose packaging sometimes expresses the amount of drug in a misleading way. For example, Pentasa (mesalamine) 250 mg capsules have been packaged in a two-capsule, unit-dose package labeled “250 mg” (see Figure 4). It is not clear to healthcare practitioners whether the entire package or each capsule contains 250 mg. Facilities in Pennsylvania have experienced this same problem, as shown in the following reports submitted to PA-PSRS.

*Patient’s medication, when scanned, indicated to give four doses. Each scanned pack was two pills, but scanned four packs and administered.*

*A nurse removed two packages (two capsules of 250 mg per package) of Pentasa from Pyxis, and the patient asked why there was two when he usually gets four. This led to some confusion.*

*A patient was administered an incorrect dose of Pentasa: 2,000 mg versus 1,000 mg.*

**Use of Color**

Color is present in many ways on the labeling and packaging of medications and is often used to draw attention to information on the label. Unfortunately, the color used on the label sometimes detracts from important information, such as the drug name and strength. Color has been used to systematically classify and identify drug classes. This technique is referred to as “color coding.” This type of system is used for ophthalmic medications in the United States; the caps and labels are color-coded according to their pharmacologic class. Practitioners who know the system can assume that a manufacturer’s vial with a yellow label means the product is a beta blocker, while a tan label means the product is an anti-infective. The effectiveness of color-coding systems depends on the practitioners’ ability to know and remember what each color represents. However, such color coding can increase the look-alike similarities of different drugs within the same pharmacologic class. Reports submitted to PA-PSRS (such as the following), as well as the U.S. Pharmacopeia-ISMP Medication Errors Reporting Program, describe confusion between these ophthalmic products.

*Three eye kits were prepared incorrectly by the pharmacist. Mydriacyl 1% (tropicamide) was supposed to be inside the kits; instead, they contained Cyclogyl 1% (cyclopentolate) drops. The nurse gave a patient the incorrect eyedrops. In others cases, the drops were corrected prior to administration. (See Figure 5 on next page.)*

Problems can also occur with color-code schemes that are applied by users, such as the American Society for Testing and Materials standard for user-applied syringe labels in anesthesiology. Some of the label colors reflect characteristics of the drug class. For example, a neon red-orange label used for neuromuscular blockers indicates “danger.” The blue signifies cyanosis of opiate-related respiratory depression. Labels for some antagonists are linked by color to the specific agonist (e.g., naloxone shares the color of opiates) but have diagonal lines printed along the border of the label. Drug names are printed on the labels, which are on rolls mounted alongside one another on a dowel so that anesthesia...
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personnel can easily retrieve the required label. Both of these scenarios demonstrate the problem when label colors identify a drug category, but do not identify a specific drug, strength, or dose contained in a syringe. The following report sent into PA-PSRS describes an error associated with the use of these labels:

At the end of cath lab case, an anesthesia resident was told to administer neostigmine to reverse the patient. The resident administered rocuronium by mistake. Investigation revealed that the attending physician and resident had drawn up the rocuronium and neostigmine prior to the start of the case. Both syringes were labeled; however, the rocuronium preprinted label is white with a red solid line, the neostigmine preprinted label is white with a red hatch-marked line. Resident mistakenly picked the syringe with the red-and-white label but did not read label prior to administration of medication.

Another example of problems associated with the use of color coding has been discussed in a previous issue of the \textit{PA-PSRS Patient Safety Advisory}, in which 10-fold overdoses of insulin occurred due to mix-ups between insulin syringes and 25-gauge tuberculin syringes.\textsuperscript{13}

In contrast to color coding, color differentiation can be used to make certain parts of the label stand out or to help differentiate one item from another. One example of this technique involves Adrenalin. The original packaging (see Figure 6 on next page) was changed after reports of delays in treatment because of the similarity in packaging between topical Adrenalin, used to stop bleeding, and injectable Adrenalin, used in emergencies such as cardiac arrest and asthma attacks. Medical personnel had unknowingly stocked their emergency box with the topical agent; when they opened the box for emergency treatment, they did not have the product they needed. They wanted the injectable form, but they identified the item by its appearance: the title (Adrenalin Chloride Solution), the distinctive white and dark-red design, the shape of the box, the horizontal bands at the bottom of the label, and the “1:1000” concentration. The distinguishing words (i.e., “Nasal Solution” and “Topical Application” versus “Injection” and “Hypodermic Use”) were relatively small and were not seen. The redesigned packaging is now distinguished by differentiating the products using a sharp color contrast.\textsuperscript{14}

Lack of Contrast
The lack of contrast in labeling can be problematic, especially on small products. One example of poor contrast leading to confusion between products involves the embossed labeling of low-density polyethylene (LDPE) ampuls of respiratory therapy medications, discussed in the June 2005 issue of the \textit{Advisory}.\textsuperscript{15}

The potential for error with this type of labeling and packaging is even greater since some manufacturers have introduced injectable products packaged in LDPE ampuls with the same type of labeling, such as heparin for IV flush and Naropin (AstraZeneca’s ropivacaine product), a local anesthetic. AstraZeneca also manufactures Naropin in various strengths (2 mg/mL, 7.5 mg/mL, and 10 mg/mL) in prefilled, Polyamp DuoFit polypropylene containers. Lidocaine is available in the polypropylene packaging as well.

![Figure 5. Two Ophthalmic Products of the Same Pharmacologic Class with Similar Packaging and Color Scheme. Image provided courtesy of ISMP.](image-url)
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These containers, which all look similar, can be mistaken for respiratory medications. It is difficult to see the small, black print placed directly on the clear plastic containers, especially when the container is held against a dark background. (See Figure 7.)

Risk Reduction Strategies
It is not enough to caution healthcare providers to be more careful because it is human nature to identify items by color, shape, type font, symbols used, and other such characteristics. To help minimize errors related to nomenclature, labeling, and packaging, consider the following strategies:

Performing a failure mode and effects analysis (FMEA). Before adding a medication to your organization’s inventory, consider gathering an appropriate interdisciplinary team to perform a FMEA to determine potential pitfalls with that medication. Including evaluation of the look-alike potential of product containers as well as possible areas of storage throughout the organization may be necessary, not just the pharmacy. Using FMEA will help identify the necessary steps to reduce the risk of errors.

Reviewing reports from external sources. Regularly reviewing professional literature may help to identify error-prone drug products.

Purchasing from different vendors. To reduce similarities and prevent errors, consider purchasing one product of an identified look-alike pair from a different vendor.

Segregating and labeling. Consider separating and/or clearly differentiating products that are similar.

Building alerts. Building alerts into computer systems may help to remind practitioners about problematic products in your organization.

Using drug dose conversion charts. Because not all healthcare practitioners are familiar with percent or ratio expressions of concentrations or adept at calculating doses of drugs whose concentrations are expressed in this manner, consider using drug dose conversion charts. It is helpful for organizations to create a dose conversion chart reflecting concentrations available in the facility. The chart can be posted on code carts and in other areas where emergency medications may be prepared. A process to ensure that these dosing charts undergo an approval process prior to use, as well as an updated review or as new products are published, can help keep these charts useful and up-to-date.

Documenting contributing factors. When submitting reports to PA-PSRS, consider taking advantage of the reporting program’s capability to track contributing factors to events. Under question 8J, “System Factors Contributing to Medication Error,” selecting an applicable item — such as “Dosage form confusion,” “Dose and identify checking (e.g., look-alike and sound-alike),” or “Label design” — may help identify products that are involved in multiple events in your facility due to the design of the label or package. Identifying these products and analyzing the contributing factors can assist your quality improvement programs and guide the development for error-prevention strategies.

Figure 6. Old Packaging for Topical and Injectable Adrenalin, Left, and the Redesigned Products, Right. Image provided courtesy of ISMP.

Figure 7. Look-Alike Packaging in LDPE Ampuls. From left, Naropin injection, cromolyn for inhalation, and ipratropium bromide for inhalation. Image provided courtesy of ISMP.
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Notes