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ISMP 25 YEARS ADVANCING MEDICATION SAFETY

Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Your attention please… Designing effective warnings

Medication-related warning systems are often used to inform both practitioners and consumers about new risks, or remind them about known risks associated with the use of medications. The warning system may ask the recipient to choose between two or more courses of action, present only one safe option, or provide information only.[1]

The warning system may also include several components that complement each other and various forms of technology. For example, the warning system for a neuromuscular blocking agent, which is intended to alert practitioners to the drug's effect of respiratory arrest and the need for ventilation, may include: a statement about the risk in the package insert; a warning statement on the carton, immediate container label, and ferrule of the vial; an auxiliary warning label on product storage locations and vials/infusions; an interactive electronic warning that requires verification that the patient will be ventilated before removing the drug from an automated dispensing cabinet (ADC); and a visual/audible warning when the product's barcode is scanned and the drug has not been prescribed for that patient. The different components of the warning system may be intended for different audiences and may be embedded in different phases of the medication use process to ensure all who are involved with the neuromuscular blocking agent are aware of this critical information.

How the components of the warning system interact and complement each other is one significant aspect of an effective medication-related warning system.[2] Another is whether the warnings truly inform practitioners about crucial medication safety issues and influence their behavior in ways intended to improve safety. While warning systems are considered mid-level strategies because they mostly involve efforts to inform and influence behavior, they can be an extremely valuable tool to help reduce the risk of potentially serious errors when they are well designed and accompanied by high-leverage, system-level risk-reduction strategies. Recommendations to improve the design, delivery, and effectiveness of medication-related warnings are discussed in further detail below.

Effectiveness of Warnings

To be effective, warnings must: 1) reach their target audience; 2) capture the attention of recipients at the right time; 3) cause recipients to understand the risk, believe that the warning relates to them, and understand the actions they need to take; and 4) lead the recipients to respond appropriately. Several design factors influence whether the warning is noticed, encoded (e.g., read/heard, understood, personalized, believed, stored in memory), and acted upon to avoid the hazard.[2,3] With few exceptions, practitioners will not typically search for or seek out warnings. Thus, warnings must be sufficiently conspicuous to capture attention, appropriately placed so their usefulness is maximized, and possess characteristics that encourage encoding of the content and action to avoid the risk.[3] If practitioners do not notice the warning, it will go unheeded; if they do not understand the risk, they might dismiss it and believe it has no importance; if they are aware of the risk but do not know how to avoid it, they might be frustrated; if they understand the risk and how to avoid it but believe the consequences are unimportant, they might not comply with the warning or may believe it is not worth the effort.[1]

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SAFETY briefs

HIGH-ALERT

Enoxaparin syringe failures. In the past few months, the US Food and Drug Administration (FDA) and ISMP have received multiple reports from practitioners and manufacturers about enoxaparin prefilled syringe failures (**Figure 1**) and inadvertent activation of the needle safety mechanism. The syringe manufacturers mentioned in the reports include Sanofi, which provides the brand, **LOVENOX**, and various generic product manufacturers (e.g., Fresenius Kabi, Winthrop, Amphastar Pharmaceuticals [IMS Limited], Sandoz, Teva [not manufacturing enoxaparin at this time]). Sanofi manufactures generic enoxaparin syringes for Fresenius Kabi and Winthrop, and is responsible for investigating associated complaints.

Figure 1. When attempting to engage the safety mechanism on an enoxaparin syringe (Fresenius Kabi), the two pieces completely separated from each other.

In 2018, 42 relevant reports were submitted by manufacturers and practitioners to the FDA Adverse Event Reporting System (FAERS). Additional events of the same nature were reported to ISMP. Of the FAERS reports, all described problems with the syringe safety mechanism, such as: the syringe broke apart when engaging the safety mechanism (n=22); the mechanism did not or was difficult to engage (n=12); and the mechanism engaged too soon (n=5).

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Over the past few decades, a sizable body of research has been amassed about how to design effective warnings.[1-10] Michael S. Wogalter, a leading international authority on warning design and use, has compiled important contributions to this field of research in a book, *Handbook of Warnings*.[3] Some of the conclusions drawn by Wogalter and other experts are provided below as examples of ways to improve the design and delivery of medication-related warnings.

Design Factors

Target audience. When designing a new warning, determine the categories of practitioners who will most likely benefit from the warning, and design it in a way that takes into account the lowest level of ability, training, and experience of the target audience.

Source credibility. Practitioners will pay more attention to warnings that stem from expert and trusted sources, and if the consequences are easily imaginable or salient.[3] If the communication appears legitimate and free of a conflict of interest, believability is enhanced, and compliance is improved.

Clinical importance. Generally, false alarms, clinically insignificant alerts, and overwarning will lead to alert fatigue and cause rational practitioners to overlook them or habitually bypass them, even if that is not the intended action. When a warning is disregarded before it can be read, it becomes completely useless. The most effective way to reach the target audience and promote understanding and compliance is to make sure the warning is clinically important.

Font size and text format. Visual warnings should be printed using bigger, bolder font sizes that are not densely compressed and are easier to read and recall.[2,3] Although bigger is generally better, what usually matters most is the font size relative to other information displayed and the contrast between the text and the background.[2] Small medication labels often do not have adequate space for effective warnings, but special extended labels can be used if necessary. White spacing between label sections enhances readability. If the warning includes distinct components, presentation in a list[2] or clustered in a tabular format[5] is more effective than in paragraph style because breaking up the information reduces cognitive effort.

Font style. Familiar sans serif fonts without embellishment, such as Helvetica, Arial, and Univers, are preferred for warning messages. Avoid fonts with serifs (short decorative lines at the start or finish of letters) such as Times New Roman unless used for small print. However, serifs are less important as long as the font style is not extreme or unusual.[3,6]

Letter case. Warnings are best presented in mixed case letters, as they are easier to read than all uppercase letters. Block-like uppercase letters look similar, especially in low lighting; lowercase letters are more unique and distinguishable.[6]

Signal words. Signal words are often used to attract attention and send a message about the hazard level. In the US, the American National Standards Institute (ANSI) recommends using:[2,3]

- **Caution** for hazards that *might* cause minor injury
- **Warning** for hazards that *might* cause serious injury
- **Danger** for hazards that *will* cause serious injury

Danger is more likely to attract attention than **Caution** and **Warning**. It conveys greater hazard and should be reserved for the most extreme cases. Other signal words that have been tested for effectiveness include (in descending order of hazard): Deadly, Fatal, Poison, Danger, Hazard, Vital, Severe, Serious, Urgent, Beware, Warning, Harmful, Caution, Alarm, Alert, Careful, Prevent, Needed, and Note.[2] Signal words can be used in either auditory or visual warnings.

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Three reports described problems with the safety mechanism but were not specific about the malfunction. Twenty-one events involved needlesticks (multiple cases in some reports), including one after the syringe had been used for a patient with human immunodeficiency virus (HIV). Three of the events were associated with underdoses; 2 involved missed doses; and 3 involved embedded needles (e.g., x-ray showed an embedded needle in one patient's abdomen). The events involved both administration by healthcare professionals (n=23) and patients (n=19). The problems are not limited to a single strength product. ISMP has asked FDA to look into the problem further.

Please advise practitioners handling these syringes to always point the needle end away from themselves and others, including the patient, until the moment of injection and after injection when activating the safety mechanism. If these syringes are dispensed for use in the home, patients should also be educated about proper use and disposal. Check with the company that supplies your enoxaparin, as some offer free educational materials and syringe disposal equipment for patients to support safe use.

Mix-ups between dexamethasone and dexmedetomidine. ISMP has received multiple reports about mix-ups between dexmedetomidine injection (sedative) and dexamethasone injection (corticosteroid). Practitioners seem to be reading the first few letters of the drug name before confirmation bias ensues. In several events, pharmacy staff selected and prepared an intravenous (IV) admixture with one drug when the other was intended, especially when an IV workflow system and/or barcode scanning verification was not used. In other cases, the drugs were stored near each other in the pharmacy, removed incorrectly to restock an automated dispensing cabinet (ADC), and placed into the wrong pockets. Nurses have also removed the wrong drug from ADCs via the override function.

Although mix-ups have happened both ways, in most cases, dexmedetomidine was selected and prepared instead of dexamethasone, sometimes for infants or children. Some incidents involved programming dexmedetomidine infusions in smart infusion

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Use only one signal word per warning to avoid confusion. It is also important to avoid indiscriminate use of signal words, particularly *danger*, *warning*, and *caution*, which may convey misleading or inaccurate hazard levels. For example, in a study that evaluated the effectiveness of electronic prescribing alerts, the signal words **Adverse Reaction**, **Interaction**, and **Low Creatinine Clearance** were used after careful consideration of *danger*, *warning*, and *caution*.[5] These clinically meaningful, patient-related words were well known, conveyed important information about the type of alert, and did not mislead the prescriber regarding the level of danger associated with the alerts.[5]

Color. Generally, the use of color can help draw attention to warnings and make them more noticeable.[2,3] The colors red, orange, and yellow help convey the hazard level, with red having the highest hazard connotation. The hazard level and urgency of the warning can also be conveyed using a combination of these colors and the ANSI-recommended signal words. Use a red background with white lettering for **Danger**, an orange background with black lettering for **Warning**, and a yellow background with black lettering for **Caution** to indicate decreasing levels of hazard (although most people find little distinction between **Warning** and **Caution**, or between orange and yellow).[2]

Message content and length. The warning must explicitly specify the hazard, the consequences of not complying with the intended course of action, and instructions for how to avoid the risk unless these instructions are obvious in the statement of risk (e.g., "**For IV use only, Fatal if given by other routes**").[1] Offer meaningful options if a decision is required, with enough information for the recipient to make an informed decision, including a brief explanation of the consequences of not following each option. The warning should be stated in short sentences or statements from the recipient's viewpoint using the active voice and familiar words without unnecessary technical jargon. Do not use abbreviations unless they have been tested by the target audience. To motivate action, the warning should be polite and engaging when possible, not intimidating and offensive.[1] Avoid vague warnings that rely on inference regarding the hazard, consequences, or desired action (e.g., high-alert medication stickers—see ***Worth* repeating...** on page 4). More explicit warnings enable the recipient to better understand and carry out appropriate actions.

Brevity is also important, and the warning should be stated concisely, presenting only enough information to avoid the hazard and/or make an informed choice.[2] The need to be explicit does not mean the warning must be long. For example, a warning on a neuromuscular blocking agent vial that simply says "**Warning: Causes respiratory arrest—Patient must be ventilated**" may be sufficient.

Affirmative wording. Whenever possible, use affirmative rather than negative statements when describing the hazard, consequences, and desired action. For example, "**For oral use only**" is more explicit and less prone to error than "**Not for IV use**" because the recipient may only see or hear the "IV use" portion of the warning statement and mistakenly believe this is the correct route of administration. Negative words in warning statements require more effort to interpret correctly and are managed in the brain apart from the rest of the words in a warning. Thus, a recipient may fail to process the negative parts of the statement and misinterpret the warning as an affirmative action.[10] This is especially possible when the warning statement on the label is partially turned or otherwise obstructed, or if the "do not" portion of the message is on one line and the rest of the message is on another.

Pictorials. Pictorials such as photographs, representative drawings, and symbols, are an exceptionally valuable tool, as they often make warnings more conspicuous and may also help communicate the content of the warning.[2,3] Recipients tend to prefer warnings that contain pictorials and notice them more quickly if the pictorials are bold, have high contrast, are simple in form, and closely represent the intended message

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pumps as dexamethasone due to look-alike product names. A large sedative overdose is possible if dexmedetomidine is administered at a rate that may be appropriate for dexamethasone, which is generally much higher. Fortunately, most reported mix-ups were identified before reaching a patient.

Use premixed dexmedetomidine (**PRECEDEX**), when available, instead of the vials. Where vials are needed, employ barcode scanning prior to IV admixture or when selecting and stocking vials in ADCs. We also recommend not storing these drugs near each other in the pharmacy. The look-alike name pair will be included on the updated ***ISMP List of Confused Drug Names***, which will be available next month on our website. We are also suggesting the use of tall man letters for dex**MEDE**tomidine and dex**AMETH**asone. We will update the ***ISMP List of Look-Alike Drug Names with Recommended Tall Man Letters*** later this year.

Administration of wrong vaccine prepared by another. A medical assistant was helping a busy nurse in a pediatric office by ushering patients into treatment rooms and checking their vital signs. For one of the patients, a pediatrician had ordered both a hepatitis B and influenza vaccine. The medical assistant brought both of the required vaccine information sheets into the treatment room to give to the child's mother, and told the nurse that she had also prepared the prescribed vaccines. Grateful for the help, the nurse assumed the assistant had completed the necessary verifications before drawing up the vaccines, then administered the vaccines to the child. When she went to document administration, she realized that, while she had correctly given the child a hepatitis B vaccine, she had incorrectly administered a hepatitis A vaccine instead of the influenza vaccine. Except during emergencies or with prefilled syringes, premixed or pharmacy-prepared intravenous (IV) solutions, and other unit dose medicines prepared in the pharmacy with the benefit of quality control mechanisms, nurses should never administer anything they have not prepared themselves. The old adage, "The nurse who measures a drug should give it" is often learned during professional training (*The Textbook of the Principles and Practice of Nursing*. 5th edition. Macmillan. New York, 1955).

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(e.g., skull and crossbones).[3] Pictorials may be especially helpful when warnings need to be communicated quickly and/or the target audience includes low-literacy or non-English readers.

Pictorials that require inference are less likely to be recognized or understood. ANSI standards suggest testing of pictorials prior to use in warnings, with a correct interpretation rate of 85% or more.[2] More importantly, the pictorial should not communicate incorrect information, and testing should demonstrate that no more than 5% of those tested are confused by the pictorial or understand it to mean the opposite of its intended message.[2] Education and exposure to associate pictorials with the related warning dramatically improves comprehension and memory.[3] Also, the use of conspicuous text *along with* pictorials enhances comprehension and recall. For example, medication instructions are recalled more easily when warnings include redundant text and pictorials.

Placement. Warnings are more likely to be noticed if placed where they are most likely to be encountered, and when the recipient will still have time to take preventive action to avoid the hazard.[1-3,5] For example, warnings placed before instructions grab the recipient's attention and result in higher compliance than warnings placed after instructions; warnings directly on a product are noticed more often than those on an outer carton; and warnings on the front of labels are more likely to be noticed than those on the back or on secondary labels.[2,3] If space for a warning is limited, adding extended labels may be necessary so the warning is located in an area where it will be noticed. Another option is to put the minimum information necessary to grab the recipient's attention on the primary label, and then direct the recipient to additional warning information in a secondary source, such as a package insert or via a hyperlink.[2]

Physical interactivity. The most noticeable and effective warnings are placed in such a way that the task is temporarily interrupted, and the recipient must physically interact with it in some way to continue.[7-9] These intrusive active warnings, also referred to as modal warnings, are not easily overridden and may involve answering questions, entering or confirming critical pieces of information, or physically removing the warning in order to proceed (e.g., warning over a port that needs to be removed before the infusion bag can be spiked). In contrast, nonintrusive passive warnings, or nonmodal alerts, do not require any special actions from recipients and are more easily overridden and less effective for alerting recipients to hazards and encouraging compliance with the desired safe behaviors. However, while interactive warnings are desirable, they are intrusive to the process and should be reserved for the most critical warnings.

Specifics for electronic alerts. Warnings presented electronically should be located within the visual field, and the main message should not require scrolling. The most critical warnings should be interactive (modal) and should shade the rest of the screen while being presented. The warning message should be presented in primary and secondary text, with the primary text always visible and no more than a sentence, and the secondary text initially hidden, if necessary, and displayed upon clicking a *More Information* link.

If the recipient must make a choice, a question should be posed below the primary warning and should always be visible. Each option should have a brief description of the action presented in larger font, along with a brief explanation, if necessary, in smaller font below the description. Because recipients are more likely to read option button labels than secondary text, it should be possible for the recipient to understand the choices by the way the buttons are labeled. The safest choice should be presented first and should be the default option (also associated with any shortcut key strokes). Secondary options that are not directly related to the question, such as *Help*, *Ignore the Warning*, or *More Information*, should be provided below the primary options.[1,5,6]

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Worth repeating...

High-alert medication stickers may not improve safety

We often receive questions related to the use of "High-Alert Medication" stickers that some hospitals apply to associated medications in their facilities. The effectiveness of these stickers as a warning is doubtful because they are not explicit regarding the hazard, the consequences, and the desired action to prevent the hazard. If the stickers are intended to simply draw attention to high-alert medications, this practice may be detrimental to your safety efforts if you affix these stickers to too many drugs or if you forget to apply them to a targeted drug. To cite an example, an error from our November 1, 2007, newsletter is *Worth* repeating...

At change of shift, a nurse noticed that a patient was barely arousable and checked his blood glucose level, which was 10 mg/dL. While administering an intravenous (IV) dose of dextrose 50%, the nurse noticed that an insulin infusion (100 units in 100 mL) intended for another patient had been mistakenly infused during the previous shift instead of a 100 mL piggyback of fluconazole. In this hospital, it was standard practice to label high-alert medications, including IV insulin, with a high-alert medication sticker, but pharmacy staff had inadvertently omitted the sticker. Without the sticker, the 100 mL bags looked very similar. The nurse, who was accustomed to high-alert stickers on insulin bags, had picked up the wrong infusion and administered it.

While the failure to place a required high-alert medication sticker on a targeted product is a proximate cause of this error, use of these auxiliary stickers are often too numerous to be effective. Placing the stickers on all or most high-alert medications will likely dilute your efforts to make the products stand out as practitioners become sensitized to the intended message. Plus, the stickers can make high-alert medications look alike, increasing the risk of selection errors. Furthermore, the stickers are vague and do not communicate meaningful information about the hazard, potential consequences, and how to avoid patient harm. Instead of using the stickers,

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Usability testing. Before implementation, warnings should undergo formal, systematic usability testing with users who might encounter the warning to assess their effectiveness,[1,5] paying attention to design features that may lead recipients to overlook, misunderstand, or ignore the warning. Use the findings to improve the warning's design before implementation. Periodically, the warning system should be reassessed to ensure it is effectively capturing attention, providing the information necessary to make them effective, and resulting in the intended action.

Perception of risk. Whether or not (and how) the recipient notices, encodes, and complies with a warning depends not only on the design of the warning but also on other factors such as the recipient's prior experiences with the perceived hazard, familiarity with the product or situation, and the cost (effort, time) of complying.[2] Practitioners who are aware of a particular hazard are more likely to notice and process a warning. While greater familiarity with one's environment and products may result in a faded perception of even well-known hazards, awareness of negative experiences and adverse outcomes associated with the hazard can heighten one's motivation to seek out and comply with warnings. Also, practitioners tend to comply with warnings more often when they observe others behaving in the same manner and when the costs of time and effort are low. For these reasons, it is crucial to maintain a high perception of risk associated with hazards by sharing internal and external stories of errors and adverse outcomes that have been linked to the hazards, modeling the desired safe behaviors associated with warning compliance, and ensuring that the effort and time to comply with warnings is as low as possible.

Conclusion

Warnings are generally less reliable than design strategies that eliminate hazards altogether, barriers that prevent hazards from touching targets, or high-level automated redundancies that detect errors before they reach targets. However, by designing more effective human-centered warnings, there's no doubt that they will help us interact with our environment more safely and will serve as a useful tool to help reduce the risk of potentially serious errors.

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specific risk-reduction strategies for each high-alert medication should be designed and implemented; if one of these strategies includes providing a warning, be sure it is appropriately designed and placed (see main article) to effectively communicate information about the hazard, consequences, and desired safety steps. If a medication requires a pharmacy-applied auxiliary label or warning, a process should be established to ensure it is applied consistently.

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ISMP has launched a new ***Gap Analysis Tool (GAT) for Safe IV Push Medication Practices***. Participants who submit their findings anonymously to ISMP by **March 31** will receive a gap analysis score and have access to aggregate data. For details, visit: www.ismp.org/node/1188.

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If you are attending the American Organization of Nurse Executives (AONE) 2019 Annual Conference in **San Diego, CA**, don't miss ISMP's midday program, ***Manage the Safety Risks Associated with IV Push Medication Use*** on **April 10.** The program, sponsored by Fresenius Kabi, will also be presented at several other national nursing meetings in April and May. To register, visit: www.ismp.org/node/1373.

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