Affirmative Warnings (Do This) May Be Better Understood Than Negative Warnings (Do Not Do That)

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A couple of years ago, the Food and Drug Administration (FDA) issued an alert reminding health care professionals that nimodipine capsules are only to be given by mouth or through a feeding tube.1 In 1996, the Institute for Safe Medication Practices (ISMP) first brought attention to serious and fatal errors caused by accidentally administering the drug intravenously after removing the contents of nimodipine capsules using a parenteral syringe and needle to facilitate oral or gastric tube administration.2 The FDA and ISMP continue to receive reports of inadvertent intravenous (IV) nimodipine administration, with serious, sometimes fatal, consequences. The FDA asks any health care practitioner who removes the contents of a nimodipine capsule using a syringe to label the syringe with the warning “Not for IV Use” to reduce the risk of accidental IV administration.

Without minimizing the FDA’s efforts to draw attention to this serious risk, ISMP suggests that further consideration is warranted when designing important warnings on pharmaceutical products and auxiliary labeling applied to products by the pharmacy. In the case of nimodipine, for example, would it be more effective to provide an affirmative warning statement, “WARNING: For Oral Use Only,” instead of the FDA’s suggested negative warning statement—“Not for IV Use”? Our concern with the negative warning statement is that the practitioner may only see the “for IV Use” portion of the warning and administer the medication intravenously. This is especially possible with a partially turned or otherwise obstructed label, or if the “Do Not” portion of the message is on one line and the rest of the message is on another line, as may occur with truncated drug entries on medication administration records. On the other hand, stating only the affirmative “For Oral Use Only” does not highlight the potential misuses of nimodipine in a way that allows practitioners to recognize quickly that they may be about to do something wrong—administer the medication intravenously.

Designing warnings is a complicated task that should be based on human factors and practice considerations. The purpose of a warning is to inform users of a new risk or remind them of a known risk. The goal of the warning is to influence behavior in a manner that best protects the user and patient. There are typically three components of an effective warning:3–5

- A signal word that helps to draw attention to the warning and quickly convey its importance:
  - Danger (or Deadly): for immediate hazards that can cause death or injury
  - Warning: for hazards or unsafe practices that can cause death or injury
  - Caution: for hazards or unsafe practices that can cause minor injury
- An explicit, necessary hazard message not subject to misinterpretation
- The consequences of the hazard and/or deviation from the warning

Human factors studies conducted outside the health care industry suggest that warning statements should be written in the active voice, not the passive voice, and, when possible, using affirmative statements instead of negative statements to ensure that people understand the meaning of the hazard, even if they don’t read every word.4,5 In several studies, active sentences were found to be verified faster than passive sentences, affirmative faster than negative, and true faster than false.4,5 The exception is a common warning instruction where a prohibition is required, such as “No Smoking.”

Negative and passive words in warning statements require more effort to interpret correctly. Statements having these features require a larger capacity of immediate memory than do otherwise identical statements lacking these negative and passive features.4,5 The negative and passive parts of the warning are encoded in the working memory of the brain apart from the rest of the words in the warning. Thus, a health care provider under stress may fail to process the negative parts of the statement—such as “Do Not”—and misinterpret the warning as an affirmative action.

Affirmative warning statements in an active voice appear to be the style of choice for many countries in the European Union and the World Health Organization (WHO). For example, the warning required on vincristine was changed from “Fatal If Given Intrathecally. For IV Use Only” to “For Intravenous Use Only. Fatal If Given By Other Routes.” The change was made to avoid association of the route, “intrathecal,” with vincristine, and to provide a positive warning statement only.

Human factors experts also suggest that consistency with the way warnings are worded is critical to facilitate detection, comprehension, and compliance with the warning.6 In the U.S., unfortunately, you can find both affirmative- and negative-style warnings on pharmaceutical products, creating an environment where health care providers don’t know what to expect, so errors of misinterpretation are more likely to occur.

ISMP urges the FDA to develop and disseminate a standard guidance on warnings utilizing human factors experts and evidence-based research where available to ensure that the most effective warnings are provided on pharmaceutical products. The goal is not to elevate the status of all drug label warnings but to remove less significant ones and standardize the

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design of the most serious warnings. Furthermore, where the risk of serious injury or death is present, the FDA should require pharmaceutical companies to rigorously test product warnings within realistic settings using clinicians who would likely encounter the warnings. Until that time, ISMP recommends the affirmative approach to warnings on labels.

References