



**Institute for Safe
Medication Practices**

a nonprofit organization

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Information and Standards Development
Nomenclature and Labeling Committee
United States Pharmacopeia
12601 Twinbrook Parkway
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Re: Petition for changes in labeling of epinephrine injection

Due to ongoing reports of serious and fatal errors associated with the clinical dosing of epinephrine injection, and confusion between epinephrine and ephedrine, the undersigned does formally request that the United States Pharmacopeia adopt changes to labeling standards for epinephrine injection and ephedrine injection.

This Petition recognizes an ongoing problem of dangerous practitioner confusion between epinephrine injection and ephedrine injection as well as ongoing confusion over the ratio method for label expression of the concentration of epinephrine injection. The petitioner requests that USP do the following:

1. Designate that epinephrine and ephedrine be labeled with enhanced letter characters (EPIneprhine and ePHEDrine).
2. Should request (1) be unacceptable, the petitioner requests that USP change the name of ephedrine injection to efedrine injection.
3. Require that, except when combined with local anesthetics, epinephrine injection concentrations be expressed only in terms of mg per mL (e.g., 1 mg/mL) and no longer expressed in terms of ratio (1:1,000; 1:10,000, etc.).

Some of the scientific facts that require action on this petition are as follows:

Regarding a name change:

1. Epinephrine and ephedrine were each introduced before existence of the 1938 Food, Drug and Cosmetic Act, and do not fall under current FDA labeling standards, providing a lack of authority for FDA to regulate these drugs.

2. The FDA Office of Generic Drugs requested manufacturers of sixteen look-alike name pairs to voluntarily revise the appearance of their established names in order to minimize medication errors resulting from look-alike confusion. The letters encouraged manufacturers to supplement their applications with revised labels and labeling that visually differentiated their established names with the use of "Tall Man" letters. Unfortunately, FDA does not have authority to act similarly with epinephrine or ephedrine, both USP drugs, not recognized under the 1938 Food Drug and Cosmetic Act.
3. The names epinephrine and ephedrine look similar and their use as vasopressors or vasoconstrictors also makes storage in similar clinical areas, such as obstetrics, very likely.
4. Both products also may be packaged alike in 1 mL glass ampuls or vials, similarities that further increase the chance of a potentially fatal mix-up. In at least one case, a mix-up occurred in part when a nurse confused ephedrine as a brand name for epinephrine⁵.
5. Mix-ups between epinephrine and ephedrine have occurred on an ongoing basis over many years⁶.
6. Research performed by the late Tony Grasha found positive correlations between enhanced letter characters in drug names and reductions in medication errors.¹

Regarding elimination of ratio expression for concentration:

1. Incidents of confusion as well as serious medication errors have been reported to the USP-ISMP Medication Errors Reporting Program where undiluted epinephrine 1:1,000 (1 mg/mL) was given intravenously to patients instead of the 1:10,000 (0.1 mg/mL) concentration. Some incidents resulted in fatalities. In each case, the more diluted epinephrine (1:10,000) was available for use, but staff inadvertently prescribed or selected the 1:1,000 concentration. Lack of understanding of the difference between the two concentrations led to these errors.
2. In a recent case, a 16-year-old male with priapism was given an intracavernous injection of 4 mg of epinephrine by a urologist who says he confused the 1:1,000 (1 mg/mL) designation and thought it meant that the drug had been prediluted (1 mg is supposed to have been diluted in 1000 mL of sodium chloride injection). The patient suffered cardiac arrest and could not be resuscitated. When referring to this expression, the reporter (who was the physician who made the error), wrote, "It is a designation from antiquity that only leads to confusion."
3. Ratio concentrations may be hard to differentiate since 1,000 may easily look like 10,000 in small print, especially when typed without the comma (1:1000 and 1:10000).
4. Studies show that these expressions are error-prone. Knowledge about concentrations expressed as a ratio or percentage is inadequate, even among physicians and emergency medicine residents²⁻⁴.
5. An inappropriate dose or life-threatening delay in treatment is quite possible, especially if these drugs are prescribed in mg (for which conversion requires prior knowledge of ratio or percent concentration and also requires calculations) or mL (a problem if multiple concentrations exist).

References:

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- (3). Jones SJ, Cohen AM. Confusing drug concentrations. *Anaesthesia* 2001;56:195-6.
- (4). Nelson LS, Gordon PE, Simmons MD, et al. The benefit of houseofficer education on proper medication dose calculation and ordering. *Academic Emergency Medicine* 2000; 1311-16.
- (5). USP Practitioners Reporting News, Similar Drug Names Reported to MER. *Issued February 25, 2004*. (6). *ISMP Medication Safety Alert!* April 17, 2003. (6). Aronson JK. "Where name and image meet" — the argument for "adrenaline." *BMJ* 2000;320:506-509.

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