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ISMP Institute for Safe Medication Practices
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Educating the Healthcare Community About Safe Medication Practices

Variable Diluted EPINEPHrine Practices and Nicknames Lead to Errors

Problem: As an alpha- and beta-adrenergic agonist, **EPINEPH**rine is a vasopressor that acts on these receptors to increase cardiac contractility, heart rate, blood pressure, and venous and arterial tone. **EPINEPH**rine is commonly used in medical emergencies such as anaphylaxis and cardiac arrest.[1] Intravenous (IV) **EPINEPH**rine is also used after dilution for a variety of other scenarios. Using low doses of diluted IV **EPINEPH**rine is traditionally associated with anesthesia practices, where it is used to rapidly address hypotension in patients with hemodynamic instability.[2] Diluted **EPINEPH**rine may also be administered during brief periods of hypotension occurring before medical procedures and to augment blood pressure in adults and children alike.[3] Diluted **EPINEPH**rine has been suggested when rapid intervention is needed to support blood pressure. In this setting, it is used as a temporary measure to limit the duration of hypotension and inadequate perfusion of vital organs.[4] While diluted **EPINEPH**rine does not treat the underlying cause of hypotension, it serves as a bridging therapy until more sustained care can be initiated, such as fluid resuscitation, blood transfusions, or a continuous vasopressor infusion.[4]

Practitioners sometimes refer to diluted **EPINEPH**rine using a variety of terms such as "low dose," "push dose," "bolus dose," "1/10th epi," "epi-sticks," or "spritzer." It is easy to understand how such a variety of terms for diluted **EPINEPH**rine can contribute to confusion and medication errors. Diluted **EPINEPH**rine doses are typically given as intermittent IV pushes, often administered every 1 to 5 minutes.[1,5] There are no commercially available formulations of diluted **EPINEPH**rine in concentrations that can be used to prepare and administer these diluted doses; however, ready-to-use products may be available from 503B outsourcing facilities. Most often, practitioners must manipulate commercially available **EPINEPH**rine products, by diluting and transferring drug and diluent to a syringe, which introduces additional risk.[4]

Practitioner confusion may also arise when using **EPINEPH**rine in emergency situations because the drug has multiple indications, each with its own dose and route of administration.[6] For example, **EPINEPH**rine auto-injectors are commonly used intramuscularly for anaphylaxis.[7] Doses from the 1 mg/10 mL products are typically administered IV for cardiac arrest and bradycardia. Doses from the 1 mg/mL and 10 mg/10 mL products are typically administered intramuscularly or subcutaneously for anaphylaxis or other hypersensitivity reactions. Or, they may be used to prepare continuous infusions, although commercially available ready-to-administer infusion products are preferred in these situations. This variety of formulations, concentrations, and routes of administration can result in medication errors such as incorrect dilution of **EPINEPH**rine, wrong dose, or wrong-route injections. Additionally, commercially available **EPINEPH**rine products typically are labeled with concentration units in milligrams per mL, but diluted **EPINEPH**rine doses may be ordered using a microgram dose-expression. This mismatch between dose units and concentration units further increases the risk of calculation and preparation errors.

A simulation study published in the *American Journal of Emergency Medicine* sought to estimate preparation and administration errors with "push dose" **EPINEPH**rine compared to pharmacist-prepared continuous infusions.[5] The study found that there were more errors associated with "push dose" **EPINEPH**rine, and dilutional errors during medication preparation was identified as the primary contributor. During the study, participants prepared 32 "push doses." Of the 32 preparations, six included a major error. Five of the six errors were related to dilution. Notably, the authors acknowledged ISMP recommendations to use ready-to-administer formulations whenever possible to decrease the risk of preparation errors.

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Demo EPINEPHrine Inadvertently Administered. A patient was receiving their second **PACL**itaxel infusion (first dose tolerated without issue) in an outpatient infusion center when they experienced redness and flushing. The nurse stopped the infusion, obtained the hypersensitivity kit, and administered a dose of intravenous famotidine per the organizational protocol. The patient's symptoms progressed, and they became unresponsive, so the nurse called emergency medical services (EMS) for higher-level care. While waiting for EMS to arrive, the nurse removed what they thought was a 0.3 mg **EPIPEN** (**EPINEPH**rine) auto-injector device from the infusion center's hypersensitivity kit and administered it intramuscularly by pressing the pen against the patient's outer thigh. Soon after, the patient awoke and became more alert. When EMS arrived and asked what medications had been given to the patient, it was discovered that the auto-injector that had been used to give the patient **EPINEPH**rine was a demonstration (demo) device intended for training purposes. The patient had not actually received any **EPINEPH**rine. The patient's clinical recovery was due to stopping the **PACL**itaxel infusion and administering the famotidine.

Mylan (Viatris) provides two yellow EpiPen devices and one gray "trainer" device in the same carton. The actual drug and demo devices are similar in shape, have a removable blue safety release end, and an orange administration end (**Figure 1**, page 2). They can easily be confused, especially during emergent situations. The infusion center staff were unfamiliar with the demo devices, and this was the first time the nurse had used an EpiPen.

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Errors Reported to ISMP

A pharmacist reported that "push dose" diluted **EPINEPH**rine is used in their organization to "normalize blood pressure." The typical process involves compounding a 0.01 mg/mL concentration by combining 1 mL of **EPINEPH**rine 1 mg/10 mL (0.1 mg/mL) with 9 mL of 0.9% sodium chloride to prepare a 0.1 mg/10 mL syringe. Doses often range from 20 mcg (0.02 mg/2 mL) to 50 mcg (0.05 mg/5 mL) with repeat doses based on the patient's response. The organization reported several errors related to this process.

*Intending to administer a 0.1 mg **EPINEPH**rine dose, practitioners removed **EPINEPH**rine 1 mg/10 mL (0.1 mg/mL) syringes from the automated dispensing cabinet (ADC) or code tray, thinking it was the diluted 0.1 mg/10 mL (0.01 mg/mL) concentration, and administered 10-fold overdoses to patients.*

*Nurses withdrew 2 mL of **EPINEPH**rine 1 mg/10 mL (0.1 mg/mL) and diluted it with 0.9 % sodium chloride to a final volume of 10 mL. This resulted in overdoses since the final concentration was 0.2 mg/10 mL (0.02 mg/mL) instead of the intended 0.01 mg/mL concentration. Similar compounding errors were made by nurses who withdrew 5 mL of **EPINEPH**rine 1 mg/10 mL (0.1 mg/mL) and diluted it with 0.9 % sodium chloride to a final volume of 10 mL, resulting in a concentration of 0.5 mg/10 mL (0.05 mg/mL).*

*A critical care physician told a nurse to "dilute 1 mL of **EPINEPH**rine with 9 mL of saline" to prepare a "push dose" **EPINEPH**rine for a patient. The nurse removed a 1 mg/mL **EPINEPH**rine vial and diluted it with 9 mL of 0.9% sodium chloride, which resulted in a 0.1 mg/mL concentration, instead of the intended 0.01 mg/mL concentration (10-fold overdose). After the nurse administered the dose, the patient's blood pressure increased more than expected, and the error was identified.*

A physician gave a verbal order to "push a dose of epi" for a patient experiencing cardiac arrest. The nurse misheard the verbal order as "push dose epi" and proceeded to prepare the 0.1 mg/10 mL "push dose" concentration, resulting in a significant 10-fold underdose. No further details about the patient's outcome or how the error was identified were shared with ISMP.

The reporting organization noted that "push dose pressors" have also become so common in the ED that one nurse questioned whether they should administer an entire 1 mg/10 mL **EPINEPH**rine syringe to a patient in cardiac arrest, since the nurse had been accustomed to administering 2 mL to 5 mL of the diluted 0.01 mg/mL preparation. In this case, the **EPINEPH**rine dose recommended in the Advanced Cardiovascular Life Support (ACLS) protocol was confused with diluted or "push dose" **EPINEPH**rine.

Safe Practice Recommendations: Organizations should consider the following recommendations.

Perform a risk assessment. Gather an interdisciplinary team comprised of prescribers (e.g., critical care, emergency medicine, anesthesia), nurses, pharmacists, and informatics practitioners to complete a risk assessment. Consider completing a failure mode and effects analysis (FMEA) to assess how **EPINEPH**rine injection is stored, ordered, prepared, administered, and referred to within the organization. Recognizing that variability may exist among practitioners and patient care units, ensure feedback is gathered from end users and review errors or close calls that have occurred, so this information can be included in the FMEA.

Develop a policy and procedure. Based on the FMEA and team consensus, develop a policy and procedure to standardize **EPINEPH**rine practices across the medication-use process within the organization for the various indications. Standardize **EPINEPH**rine storage locations and naming conventions that clearly state drug, dose, concentration, and diluent in all systems.

Leverage the EHR. Use the risk assessment to understand which patient populations may likely require low doses of diluted **EPINEPH**rine and build these orders into the appropriate order sets in the electronic health record (EHR). Maximize clinical decision support to guide prescribers to select the correct **EPINEPH**rine option based on the indication, incorporate dose range checking, and automatically link the appropriate concentration within the pharmacy system.

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Figure 1. The Mylan (Viatris) 0.3 mg EpiPen carton contains two EpiPen auto-injectors and a similar-looking trainer device.

Another organization reported a similar concern with Teva's 0.15 mg **EPINEPH**rine auto-injector (for patients weighing 15 to 30 kg), which includes two green **EPINEPH**rine auto-injector devices and one gray trainer device within the same carton (**Figure 2**). After opening the carton, the blue safety release ends on both devices look identical (**Figure 3**), and not knowing it was a trainer device, a pharmacy technician loaded the demo product into the BoxPicker automated storage system along with active medications. Fortunately, the error was identified by a pharmacist. The organization reported that they now open each **EPINEPH**rine auto-injector carton after receiving the shipment and discard the trainer device.

Figure 2. The Teva 0.15 mg **EPINEPH**rine injection carton contains two **EPINEPH**rine auto-injectors and a similar-looking trainer device.

Figure 3. Upon opening the carton, the blue safety release ends on both the actual medication device and the trainer are identical.

We wrote about a very similar scenario in our February 27, 2014 article, Trainer EpiPen Used During Code. At that time, ISMP had asked Mylan to offer a purchasing option that does not include trainer devices. However, the last

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Provide ready-to-administer products. Use commercially available ready-to-administer **EPINEPH**rine products.[8] If a diluted concentration of **EPINEPH**rine is required, avoid bedside preparation by practitioners. Consider purchasing the diluted product from 503B outsourcers or having pharmacy prepare and dispense diluted **EPINEPH**rine in a ready-to-administer form. Evaluate alternative vasopressors that are commercially available in diluted concentrations or in ready-to-administer products (e.g., phenylephrine).

Standardize labeling of prepared dilutions. If **EPINEPH**rine must be diluted by practitioners, consider creating kits that contain clear instructions, required medications, diluents, syringes, and preprinted labels to help reduce incorrect product selection, dose calculation, or labeling errors.[4] The quantity of **EPINEPH**rine per total volume in the syringe or IV bag should be the primary expression on the container label, followed by quantity per milliliter enclosed by parentheses (quantity/mL). Also, consider if practitioner-prepared dilutions should require an independent double check.

Assess storage. Evaluate **EPINEPH**rine storage locations, including in the pharmacy and in ADCs, trays, and kits. Store medications in standard configuration, with labels facing up, and physically separate look-alike products to reduce selection errors.

Never dilute in 0.9% sodium chloride flushes. Never dilute or reconstitute any IV push medication by drawing the medication into a commercially available prefilled flush syringe of 0.9% sodium chloride.[8] This practice has led to medication-containing saline flush syringes mistaken as plain saline flush syringes.

Do not abbreviate. When ordering or discussing diluted **EPINEPH**rine preparations, do not use nicknames. Always communicate the full drug name, dose, concentration, diluent, route, and indication. Coach staff to clarify the full medication order if another practitioner uses an abbreviation or nickname.

Limit verbal orders. Limit the use of verbal orders to true emergencies. When a practitioner receives a verbal order from a prescriber, they must repeat back the complete order and seek clarification, as needed.

Require an indication. Ensure all orders, including verbal orders provided during emergent situations, include an indication and ensure it aligns with the patient's clinical condition. The person receiving the order should ask for clarification if the order does not make sense.

Optimize barcode scanning. Use barcode scanning when preparing **EPINEPH**rine in intravenous workflow management systems (IVWMS), when refilling ADCs, and prior to medication administration.

Educate staff. Provide initial and annual competency assessments for practitioners who prescribe, verify, dispense, prepare, and administer **EPINEPH**rine. Use simulation-based education to achieve specific learning objectives, including appropriate **EPINEPH**rine selection, preparation, administration, and dosing based on clinical indications. Encourage staff to report errors internally and to ISMP for shared learning.

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time we spoke with the company (now Viatris), we learned it plans to continue packaging the drug as is for now. The company also told us that individual pens do not need to be stored in their cartons. Therefore, we highly recommend removing trainer devices from the carton and either discarding or storing them in a classroom/training area, and not in patient care areas. Affix auxiliary labels on all simulation supplies (e.g., Not for human use, Education only) and have educators account for every demo product used during training. A redesign considering human factors is recommended to better distinguish trainer devices from those containing medication. Generic **EPINEPH**rine auto-injectors are available without a trainer device, and **AUVI-Q** (**EPINEPH**rine), the "talking" auto-injector, is distributed with a trainer that verbally announces it contains no needle or drug. If you suspect that any training products may have been or were almost administered to a patient, report it to ISMP.

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