

May 24, 2018



This alert is based on information from the National Medication Errors Reporting Program (MERP) operated by the Institute for Safe Medication Practices (ISMP).

Safe handling of concentrated electrolyte products from outsourcing facilities during critical drug shortages



Given the near total lack of availability of potassium chloride for injection concentrate in vials (2 mEq/mL), along with problems accessing the 250 mL pharmacy bulk package (2 mEq/mL), some healthcare providers have benefited from outsourcing facilities that have compounded this product starting with the active pharmaceutical ingredient (API). However, outsourcing facilities are not subject to all of the same labeling requirements that are mandated for commercial manufacturers for potassium chloride injection concentrate or any pharmaceutical product. Occasionally, this has led to labeling or packaging that is unusual or unfamiliar to certain healthcare providers, which increases the risk of a serious medication error.

Recently, two examples have come to our attention. An outsourcing division of Nephron Pharmaceuticals provides compounded potassium chloride for injection concentrate in a syringe. The syringe is intended for pharmacy use only to further dilute for central or peripheral intravenous (IV) administration. However, one can envision ways these syringes could inadvertently reach patient care units and be mistaken as a medication intended for direct IV administration given its packaging in a syringe. Direct IV administration of potassium chloride for injection concentrate has proven fatal.

The other example involves potassium chloride for injection concentrate packaged in vials by Premier Pharmacy Labs, also an outsourcing facility. This drug is packaged in an amber glass vial with a black cap with the warning, "Must be diluted." However, the vial does not have a black ferrule with this statement, as required by USP General Chapter <7> of commercially available vials of potassium chloride for injection concentrate. Also, when

the black cap is removed from the vial of the compounded potassium chloride for injection concentrate, it looks remarkably similar to the Premier Pharmacy Labs' vial of calcium chloride. Although the product labels include an NDC number and barcode, both amber vials have the same pattern of red and white on the labels along with plain aluminum ferrules (**Figure 1**), which could contribute to a dangerous mix-up.

Other labeling and packaging problems have been reported with products compounded by outsourcing facilities. For example, the strength per mL is sometimes the most prominent expression on the principal display panel of an outsourcing facility's product label, rather than the strength per total volume (followed by the per mL amount in parentheses), as required by USP and the US Food and Drug Administration (FDA) for commercial manufacturers.

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Figure 1. Potassium chloride for injection concentrate vial (left) comes with a black cap, but once removed, it looks similar to calcium chloride vials (right). Premier Pharmacy Labs is investigating ways to reduce look-alike vial appearances. Although not visible here, an NDC number and barcode are printed elsewhere on the labels.

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The National Alert Network (NAN) is a coalition of members of the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP). The network, in cooperation with the Institute for Safe Medication Practices (ISMP) and the American Society of Health-System Pharmacists (ASHP), distributes NAN alerts to warn healthcare providers of the risk for medication errors that have caused or may cause serious harm or death. NCCMERP, ISMP, and ASHP encourage the sharing and reporting of medication errors both nationally and locally, so that lessons learned can be used to increase the safety of the medication use system.

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Safe handling of concentrated electrolyte products continued from page 1

We recognize that outsourcing facilities such as Nephron, Premier Pharmacy Labs, and others are trying to expedite products to alleviate pharmaceutical shortages. However, this can cause unintended consequences such as unsafe labeling and packaging and variability in the way critical information is expressed on labels, which can lead to serious errors. Thus, ISMP has asked FDA to convene an FDA Pharmacy Compounding Advisory Committee meeting to discuss medication errors related to the labeling and packaging of products from outsourcing facilities and to inform the next steps. These next steps might include an FDA guidance on labeling and packaging for outsourcing facilities, requiring outsourcing facilities to follow current USP or FDA labeling and packaging standards, or some other strategy that prevents outsourcing facilities from following different container labeling standards than commercial manufacturers.

Until then, healthcare providers should consider the following recommendations:

- Whenever possible, only use commercial FDA-approved products or, when necessary, products from outsourcing facilities that follow USP <7> labeling standards.
- Anticipate unexpected differences in the labeling and packaging of products from outsourcing facilities given the lack of guidance on these topics from FDA.
- Assess the labeling and packaging of all products from outsourcing facilities for safety. If the product is a high-alert medication, consider conducting a streamlined failure mode and effects analysis (FMEA).
- Take steps to reduce the risk of errors if critical vulnerabilities with labeling and packaging have been identified with an outsourcing facility's product during assessment. For example, circle "potassium" or "calcium" to draw attention to the drug name on look-alike vials, or add an auxiliary label that clearly provides necessary information.
- Embed safety strategies for potassium chloride for injection concentrate and other concentrated electrolytes such as magnesium sulfate injection, calcium chloride injection, and sodium chloride injection greater than 0.9%. Potassium chloride for injection concentrate must never leave the pharmacy undiluted. Consider appropriate restrictions for other concentrated electrolytes as well.
- Communicate with staff about drug shortages. If switching from a commercial product to an outsourcing facility product, notify all practitioners potentially impacted by the switch and alert them to any differences between the products, labeling and packaging issues, and steps the organization is taking to reduce the risk of errors. Include product photographs whenever possible.
- Employ barcode scanning technology to verify that the correct medication has been selected prior to dispensing and/or administration, including during pharmacy compounding. Otherwise pharmacists will need to rely on manual independent double checks.
- Report all errors and safety concerns associated with the labeling and packaging practices of outsourcing facilities to ISMP (www.ismp.org/merp) and FDA (www.fda.gov/Safety/MedWatch/).



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