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ISMP
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Acute Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

Survey exposes risks with custom and multi-chamber bag parenteral nutrition—Part I

Problem: Parenteral nutrition (PN) is a complex life-sustaining therapy for patients who cannot intake adequate oral or enteral nutrition. It can contain more than 40 ingredients and is considered a high-alert medication. Pharmacy can compound PN specifically for a patient (i.e., custom PN), or it can be delivered using commercially available multi-chamber bag parenteral nutrition (MCB-PN). MCB-PN products are available in two- or three-chamber bags. **CLINIMIX** and **CLINIMIX E**, manufactured by Baxter, are available with two chambers. Clinimix comes with one chamber containing amino acids and the other containing dextrose, and Clinimix E comes with one chamber containing dextrose with calcium and the other containing amino acids with electrolytes. **KABIVEN** and **PERIKABIVEN**, manufactured by Fresenius Kabi, are available with three chambers, each holding one of the following: dextrose, amino acids and electrolytes, or injectable lipid emulsion (ILE). For all MCB-PN products, practitioners must break the seals that separate the chambers and mix the chamber contents to ensure complete activation prior to administration. While these products require fewer compounding steps, the pharmacy may still add additives (e.g., multivitamins, trace elements) in a sterile environment prior to administration.

In our July 28, 2022 article, *Multi-chamber bag parenteral nutrition is not without risk*, we shared an increase in the number of errors and workarounds related to the shortage of PN components. To conserve resources, some organizations were forced to reduce the number of days they provided PN to patients. For example, an organization reported they had to reduce the administration of PN to three times per week rather than daily. In other cases, organizations used alternative products such as MCB-PN for patients instead of patient-specific compounded PN.

Some of the error reports submitted to ISMP involved mix-ups between MCB-PN bags. For example, during a shortage of PN compounding ingredients, one organization purchased Clinimix E 4.25/10 (dextrose with calcium and amino acids **with** electrolytes) as well as Clinimix 4.25/10 (dextrose and amino acids **without** electrolytes). The organization reported multiple errors in which the wrong formulation was dispensed, which was attributed to similar-looking packaging as well as staff unfamiliarity with these products. Other events were related to the failure to activate the MCB-PN bags. This resulted in the omission of certain components of the PN, such as dextrose and calcium. Organizations have also reported errors with patient-specific compounded PN involving all steps of the medication-use process. The complexity of these processes, combined with a lack of adherence to safe PN practices, has led to harmful outcomes and fatalities. To gain insight into the existing challenges, ISMP conducted a survey between December 2024 and January 2025. Details from the survey follow.

Respondent Profile

There were 280 respondents who completed our survey. Most respondents were pharmacists (79%), followed by nurses (10%), pharmacy technicians (4%), dietitians (4%), prescribers (2%), and others (1%). More than a quarter (26%) worked at hospitals with 100-299 beds; 25% with 300-499 beds; 22% with 500 beds or more; 10% with 26-99 beds; and 5% with 25 beds or less. The remaining respondents (12%) indicated this was not applicable based on their practice setting. Practitioners worked in various settings including community hospitals (38%), teaching hospitals (28%), critical access hospitals (8%), home infusion (6%), pediatric hospitals (4%),

continued on page 2 — Parenteral nutrition >

SAFETY briefs

HIGH-ALERT

Infusion errors can still occur with interoperability. A hospital recently implemented interoperability between their electronic health record (EHR) and smart infusion pumps. For a patient with atrial fibrillation, a prescriber ordered dextrose 5% water (D5W) to infuse at 75 mL/hour as a maintenance intravenous (IV) fluid, and amiodarone (450 mg/250 mL in D5W) to infuse at 0.5 mg/min (16.7 mL/hour). To initiate the infusions and EHR documentation, the nurse scanned the patient's identification (ID) band, infusion pump, and barcode on the D5W bag. She then scanned the patient's ID band, a second infusion pump channel, and the pharmacy label barcode on the amiodarone bag to initiate that infusion and document administration. Later, the prescriber increased the D5W maintenance infusion rate to 100 mL/hour. Around the same time, the patient's amiodarone infusion was nearly completed, so the nurse obtained a replacement bag from the pharmacy.

During the EHR barcode scanning steps to associate the new amiodarone bag with the infusion pump, the nurse scanned the patient's ID band, the pump channel that was infusing amiodarone, and a barcode on the amiodarone infusion bag. The pump generated an alert, "Channel is currently infusing," with error details, "Stop the channel or use a different channel and resend the order details to the pump." To resolve this, the nurse stopped the current infusion of amiodarone and cleared the pump settings. She then restarted the process by scanning the patient's ID band, the pump, and a barcode on the amiodarone infusion bag, and did not receive any alerts on the pump. However, an EHR alert was generated stating "This pump is associated to a different order." Not understanding what the alert meant and/or due to alert fatigue, the nurse bypassed the warning and initiated the infusion.

It turned out that the nurse had scanned the manufacturer's barcode on the diluent bag (D5W) that the pharmacy used to compound

continued on page 2 — SAFETY briefs >

> Parenteral nutrition — continued from page 1

cancer care hospitals (3%), long-term care facilities (2%), women and children hospitals (1%), and other practice locations (10%) (e.g., ambulatory care practice settings, rehabilitation hospitals, compounding pharmacies, industry, pharmacy benefits management). Most practitioners (87%) were from the United States.

MCB-PN Use

Of the 53% of respondents that stated they use MCB-PN in their organization, a little more than a quarter (26%) use it for all patients needing PN, while approximately a third (34%) use it for less than 25% of their patients. One in ten (10%) were unsure of the percentage of patients that receive MCB-PN at their organization. However, more than one-third (34%) said their organization has increased the use of MCB-PN in the past 3 years due to drug shortages.

Respondents told us that MCB-PN products are always stored/dispensed from pharmacy (91%) or from a combination of pharmacy and automated dispensing cabinets (ADC) (8%). For others (2%), MCB-PN is stored in a locked cabinet for nurses to access or are only used as an ingredient on the automated compounding device used in pharmacy. When it comes to who activates MCB-PN (i.e., mixes the chambers), this is most often done by pharmacy in a sterile environment (50%) but not always (24%). Others responded that this is done by a combination of pharmacy and nursing (11%), always by nursing (11%), or by patients/nurses in the home (4%).

When asked what components may be added to MCB-PN prior to dispensing, additives included the following: multivitamins (83%), trace elements (77%), electrolytes (52%), other medications (30%) (e.g., regular insulin, heparin, histamine antagonist), ILE (15%), dextrose (13%), and amino acids (15%). Some (12%) respondents indicated their organizations do not add any additives.

Errors with MCB-PN

In the past 3 years, nearly one-third (29%) of respondents have experienced or are aware of a close call (did not reach the patient) or medication error that reached a patient and involved MCB-PN. Respondents provided descriptions of more than 40 errors. Examples include the following: pharmacy or nurses forgetting to activate the bag resulting in administration from only one chamber; mix-ups between nearly identical-looking formulations; wrong patient errors after barcode scanning was bypassed; incorrect rate of infusion; a formulation that is only approved for central line administration ordered for a patient who only had peripheral access; failure to add prescribed additives (e.g., multivitamins, trace elements); and adding the incorrect amount of ingredients (e.g., 100 units of insulin added instead of the prescribed 10 units). One respondent said they do not have a clear process for documenting when additional electrolytes have been added to the MCB-PN. Another practitioner told us that their pharmacy only purchases Clinimix E, but due to a shortage, the buyer was purchasing any product that was available. In this case, although the orders were for Clinimix E (**with electrolytes**), Clinimix (**without electrolytes**) was dispensed to multiple patients over several weeks until a nurse identified the error.

Some practitioners told us that most of the medication errors that occurred in their organization were related to infusing a MCB-PN bag beyond the intended 24 hours since the bag volume exceeded the prescribed dose-rate for a 24-hour period. In one case, a prescriber ordered Clinimix with additives to infuse at 35 mL/hour on day 1. The prescriber ordered the same formulation on day 2 at a rate of 45 mL/hour. According to the prescribing information and hospital policy, the MCB-PN bag should have been discarded after infusing for 24 hours and a new bag initiated on day 2. However, the nurse increased the infusion rate of the bag that was infusing (from day 1) instead of replacing the bag. This error was discovered on day 3, when another nurse identified an additional error; the lipids were infusing without a filter via a Y-site on the administration set. The patient suffered an embolism.

continued on page 3 — Parenteral nutrition >

>SAFETY briefs

cont'd from page 1

the amiodarone rather than the pharmacy-generated barcode identifying the compounded amiodarone product. The EHR associated the "D5W" scan (actually the amiodarone bag) with the D5W maintenance infusion order and disassociated the prior D5W maintenance infusion. Since the disassociation was not a discontinuation of the infusion, the D5W maintenance infusion continued to infuse at 75 mL/hour instead of 100 mL/hour as ordered. However, the associated amiodarone in D5W was administered at 100 mL/hour instead of the ordered rate of 16.7 mL/hour.

Approximately 2.5 hours later, the pump alarmed that the infusion bag had reached the volume to be infused (250 mL), and the nurse identified the error. The patient became hypotensive, a rapid response team was activated, and the patient was treated with IV fluids. However, the patient died the following day. Although the error was determined to not be the immediate cause of the patient's deterioration, it may have potentially exacerbated their underlying illness.

The organization identified several contributing factors: medication labeling issues resulting in multiple scannable barcodes on the infusion bag as well as staff unfamiliarity with the new interoperability technology and how to respond to alerts.

We warned about a different type of error related to an infusion bag having more than one scannable barcode in our April 4, 2024 article, *Patient found unresponsive after Zosyn label placed on Myxredlin bag was infused.* In this case, the pharmacy inadvertently added a patient-specific label with a barcode for **ZOSYN** (piperacillin-tazobactam) to a premixed infusion bag of **MYXREDLIN** (insulin human). The nurse scanned the barcode on the pharmacy label, which led to the administration of the incorrect medication (Myxredlin instead of Zosyn). Both products were commercially available. In situations where commercially available premixed infusions are used, practitioners should scan the manufacturer's barcode printed directly on the product, not the barcode on the pharmacy-applied label. This ensures that the right (or wrong) container is in hand to prevent the risk of a false positive

continued on page 3 — SAFETY briefs >

> Parenteral nutrition — continued from page 2

MCB-PN Competency Assessment

More than two-thirds (66%) of the respondents indicated that their organization does not provide an initial and/or annual competency assessment for any practitioners who prescribe, dispense, activate, and/or administer MCB-PN. For organizations that provide education, they reviewed how to activate the MCB-PN bag (71%); how to calculate the amount of macronutrients, electrolytes, and additives patients will be provided from a MCB-PN bag in a set timeframe (49%); the stability data for any pharmacy additives and where this information is available for practitioners (39%); and how to enter orders for MCB-PN in the electronic health record (EHR) (34%). For those who reported other forms of education (30%), training was provided for order verification, compounding, and/or a basic clinical overview of PN.

Custom PN Use

More than three out of four (78%) respondents indicated that their organization provides custom PN. In those cases, custom PN is compounded on-site (59%), outsourced (35%), or a combination of on-site preparation and outsourced (6%). Less than one-half (49%) of respondents work in organizations that have an interface between the EHR and automated compounding devices to avoid transcription of orders. Unfortunately, less than one-half (48%) of respondents were aware of an organizational process for the pharmacy or prescriber to work with the patient's home infusion pharmacy when PN orders need to be converted from MCB-PN to a patient-specific compound. When this is done, less than two-thirds (59%) require an independent double-check of all calculations to verify accuracy.

Errors with Custom PN

In the past 3 years, 40% of respondents have experienced or are aware of a close call or a medication error that reached a patient that involved a custom PN product. Respondents provided descriptions of more than 80 errors. Examples include the following: multiple errors when transcribing the order from the EHR to the automated compounding device (e.g., conversion errors between percent [%] versus g/kg, mEq/L versus mEq/kg); products set up incorrectly in the compounder (e.g., incorrect mEq amount entered for a new manufacturer); failure to add prescribed additives; adding the incorrect amount of additives; or adding incorrect additives (e.g., iron sucrose rather than iron dextran, insulin lispro rather than regular insulin, potassium chloride rather than potassium phosphate). There were also reports of PN precipitation due to miscalculation of calcium and phosphorus amounts. In a more serious case, pharmacy added too much calcium and phosphorus to a bag, which precipitated out of the solution and resulted in a patient's death.

Administration errors included wrong patient errors, nurses stopping the PN infusion without notifying other practitioners, and multiple wrong rate errors (e.g., cyclic rate not infused as prescribed, forgetting to change the infusion rate after an order has been modified, ILE infused at PN rate and PN infused at ILE rate). In some cases, this led to electrolyte imbalances, hypoglycemia, and elevated triglycerides. One practitioner shared that after PN was discontinued abruptly without subsequently providing maintenance fluids with dextrose, the patient experienced hypoglycemia. Another told us there were times when the home care pharmacy used a significantly different patient weight than what the clinic had documented, resulting in the patient receiving the incorrect dose of PN components.

Others shared concerns about the impact of shortages of PN components. In one case, a patient received PN without the required multivitamins (with thiamine and folate only) due to a shortage. After the shortage was resolved, multivitamins were not restarted in the PN. The patient later suffered from broken bones and severe vitamin D deficiency.

continued on page 4 — Parenteral nutrition >

>SAFETY briefs

cont'd from page 2

barcode scan from an incorrectly applied pharmacy label.

Errors like this call for an evaluation of your policies and procedures regarding how labels with barcodes are placed on infusion bags. Consider completing a failure modes and effects analysis (FMEA) to determine if it is possible to remove the pharmacy-generated barcode from pharmacy labels placed on commercially available premixed products, to force scanning of the manufacturer barcode. Just as important, evaluate your process when pharmacy compounds an infusion, and consider covering the manufacturer's barcode before dispensing, which the organization involved in the error described above has begun to do, so that the nurse scans the barcode on the patient-specific label and not the manufacturer barcode on the diluent bag.

Vendors should ensure alert messages are intuitive so that practitioners can understand the warning and take appropriate action. Prior to implementing interoperability, a team should proactively identify and address potential issues and barriers. During initial and annual competency assessments, educate practitioners about the proper use of interoperability, including what alert messages mean and how to respond appropriately. Provide simulations of the required steps (e.g., after scanning make sure to review the pump settings and the order populated in the EHR, review and respond to any alerts). Regularly monitor interoperability compliance data, including alerts and actions taken in response. If there is uncertainty around what an alert means, encourage practitioners to escalate the concern and clarify prior to administering the medication. Provide feedback to vendors if an alert is not clear. Gather feedback from end users, and incorporate lessons learned from close calls and errors that reach patients, including this case, so you can address any issues/barriers.

HIGH-ALERT

Esmolol labeled as "DOUBLE STRENGTH" may lead to confusion. A pharmacist reported concerns with the labeling of esmolol 2,000 mg/100 mL premixed bags made by WG Critical Care. The label states, "Esmolol Hydrochloride in Sodium Chloride Injection DOUBLE STRENGTH" in green font with the

continued on page 4 — SAFETY briefs >

> Parenteral nutrition — continued from page 3

Custom PN Competency Assessment

More than half (53%) of the respondents indicated that their organization does not provide an initial and/or annual competency assessment for any practitioners who prescribe, dispense, compound, and/or administer custom PN. Respondents who work for organizations that provide education noted that they review how to calculate the amount of macronutrients, electrolytes, and additives patients will be provided from a custom PN bag based on the ordered rate of infusion (81%); how to enter orders for custom PN in the EHR (61%); the stability data for any pharmacy additives and where this information is made available for practitioners (60%); and procedures related to use of an automated compounding device (40%). Those who reported other forms of education (14%) included several weeks of pharmacist training alongside a PN pharmacy specialist before being approved to write PN orders through a collaborative practice agreement, and instruction on how to monitor patients receiving PN.

Standardized Cutoff Times

Eighty percent of respondent organizations have standardized cutoff times for PN ordering and preparation. Staff usually (58%), always (30%), sometimes (9%), or rarely (3%) adhere to the established times. In our April 21, 2011 article, *Another tragic parenteral nutrition compounding error*, we discussed an event that occurred after a premature infant's PN order was faxed to the pharmacy after midnight. The pharmacy transposed doses of sodium (14.7 mEq) and calcium (982 mg) after the pharmacist entered them into the automated compounding device software, resulting in a 60-fold error in the sodium dose. The infant experienced cardiac arrest and died. Among several contributing factors, not having the appropriate staff to safely prepare and double-check PN components after hours contributed to the error.

Additional Feedback about PN

The following are examples of **PN-related safety concerns** that respondents shared:

Practitioners need to have a better understanding of the stability of PN products when components are added.

Orders in the EHR are generic (i.e., central PN, peripheral PN) and do not screen for drug-drug interactions with the various additives, or duplicate therapy.

Cyclic PN and/or unplanned interruptions or abruptly stopping PN that contains large amounts of electrolytes and/or insulin (e.g., patient going to surgery) are always worrisome as providers may not immediately appreciate how much IV supplementation is needed when nutrition is stopped.

Unfortunately, in my area, there is no consistency regarding how we receive or send the PN information to the next facility during transitions of care. We have had two patients in the past year who were home PN patients who did not disclose this information, and it was not recognized until well into the hospital stay that PN was needed. One of the patients was admitted with a line infection, and her peripherally inserted central catheter (PICC) line was removed before it was even discovered she was on home PN.

The following are **MCB-PN-related safety concerns** that respondents shared:

We found the use of MCB-PN convenient and worked well for most patients (greater than 90%). However, its use becomes challenging when patients have fluid restrictions as we cannot customize the volume.

continued on page 5 — Parenteral nutrition >

>SAFETY briefs

cont'd from page 3

concentration to the right (**Figure 1**). However, there is no approved standard concentration upon which "double strength" of esmolol injection should be based. This may not match what is considered "double concentration" at all institutions. There may be a risk of errors if practitioners refer to a concentration as standard or double strength without communicating the actual concentration.

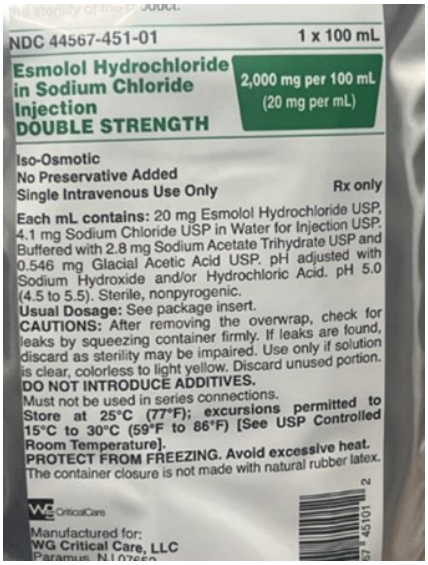

Figure 1. Esmolol label that includes the words "DOUBLE STRENGTH" as a prominent part of the labeling.

We have received similar reports where practitioners have been confused by this terminology. In one case, a nurse programmed an infusion pump as ni**CAR**dipine 100 mg/250 mL (0.4 mg/mL), but the infusion bag contained ni**CAR**dipine 40 mg/200 mL (0.2 mg/mL). This organization's standard ni**CAR**dipine concentration was 0.2 mg/mL and the pharmacy used "double strength" as a concentration descriptor when they compounded 0.4 mg/mL ni**CAR**dipine infusions. The 0.2 mg/mL concentration is commercially available in a premixed bag with the carton label highlighting that it is a "double concentration" as the manufacturer also provides a 0.1 mg/mL product (**Figure 2**, page 5). When the nurse read the manufacturer's packaging concentration descriptor of "double concentration" on the 40 mg/200 mL (0.2 mg/mL) product, they selected the double concentration entry in the infusion pump, which was actually the 0.4 mg/mL option, resulting in an underdose.

continued on page 5 — SAFETY briefs >

> **Parenteral nutrition** — continued from page 4

The concentrations of MCB-PN available become a challenge for patients who have edema and start having pulmonary or cardiac complications.

MCB-PN bags are frequently not available due to shortages.

There is confusion regarding the use of in-line filters related to MCB-PN.

Clinimix and Clinimix E formulations look very similar with the exception of E on the label. SMOFlipid and Intralipid also look very similar. It would be great for the products to be designed to better differentiate them from one another to avoid mix-ups.

The following are **PN-related competency concerns** that respondents shared:

Lack of emphasis on PN education in pharmacy schools.

There is not a great understanding of PN in newly trained pharmacists. It is not something required in the curriculum of pharmacy schools, so many new practitioners have very little exposure to it. This is concerning for the risk of errors when pharmacists go to institutions that routinely do PN.

Lack of pharmacist training in electrolyte adjustments.

There is a general lack of training for pharmacists within our organization regarding topics like osmolarity, nutrients, compatibilities, etc.

Technicians are mainly compounding PN, are they trained? Not particularly. They need to be.

Conclusion

Thank you to all who responded to the survey. Your insights are invaluable in making healthcare safer for all. In the next issue of this newsletter, we plan to publish a follow-up article (**Part II**) describing how organizations can learn from these survey results and take action to prevent PN-related errors.

Special Announcement

ASHP free webinars

The American Society of Health-System Pharmacists (ASHP) is offering **FREE** webinars: *Achieving Your Personnel Best: Training Personnel in USP Chapter 797 and Opportunities for Quality Assessment Plans*, on **April 8, 2025**, which will address the changes to USP <797>; and *IV Been There Too: Safely and Effectively Incorporating Technology and a Designated Person in USP <797> Compliance*, on **April 22, 2025**, which will describe opportunities to implement and validate technology for sterile compounding and highlight an example of incorporating a designated person and their experiences. Continuing education (CE) credit is available for pharmacists and technicians. For more information about each webinar and to register, please click on the program titles.

>SAFETY briefs

cont'd from page 4

We notified the US Food and Drug Administration (FDA) of the risk of medication cartons and infusion labels stating double strength or double concentration. While the FDA does not currently recommend use of the term "double strength," the statement on this generic esmolol label originates from the approval of the original brand product. Organizations should assess the risk of using commercially available premixed infusions with this terminology on the label.

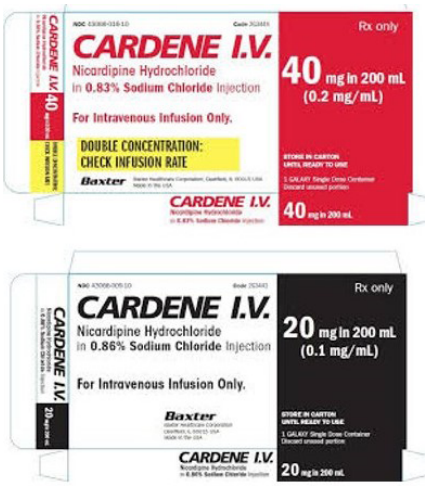

Figure 2. An example of a ni**CAR**dipine (**CARDENE**) 40 mg/200 mL (0.2 mg/mL) product with "double concentration" on the carton (top) to differentiate it from the 20 mg/200 mL (0.1 mg/mL) product (bottom).

Avoid using terminology such as "standard strength," "double strength," or any other multiple as a descriptor in all systems (e.g., electronic health record, automated dispensing cabinet, infusion pump), on pharmacy-prepared infusion labels, and when communicating concentrations. When possible, provide commercially available, premixed medication infusions in a standard concentration. If compounding is needed, provide standard drug concentrations and refer to the American Society of Health-System Pharmacists (ASHP) *Standardize 4 Safety* initiative. Report close calls and errors that reach patients to your organization's error reporting program and ISMP.

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