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Parenteral Nutrition Electrolyte and Mineral Product Shortage Considerations

ASPEN has developed parenteral nutrition (PN) shortage considerations in order to assist its members and other clinicians in coping with PN shortages for their patients. These recommendations are approved by the ASPEN Clinical Practice Committee and the Board of Directors.

For the most up-to-date supply information, see these websites:

- American Society of Health-System Pharmacists (ASHP), Drug Shortages Resource Center
- U.S. FDA Drug Shortages
- ASPEN Latest News and ASPEN Product Shortage Latest News

Important Note:

These recommendations do not constitute medical or other professional advice and should not be taken as such. To the extent that the information published herein may be used to assist in the care of patients, the primary component of quality medical care is the result of the professional judgment of the healthcare professionals providing care. The information presented here is not a substitute or replacement for the exercise of professional judgment by healthcare professionals; rather, it is intended to supplement professional training and judgment. Circumstances and patient specifics in clinical settings may require actions different from those recommended in this document; in those cases, the judgment of the treating professionals should prevail. Use of this information does not in any way guarantee any specific benefit in outcome or survival.

These shortage recommendations are intended only for use during product shortages, when adequate product is unavailable. These measures are not ideal for ensuring safe and optimal patient care and should not be considered standard practice. Any deviation from manufacturer-recommended practices should be temporary and reversed once adequate product supply is restored. No single strategy will work for all organizations. Institutions must carefully evaluate each option, weighing potential risks and benefits before implementation. These recommendations are provided with the understanding that they are followed at the institution's own risk, and each organization assumes responsibility for any resulting outcomes.

Questions regarding these recommendations should be directed to clinicalpractice@nutritioncare.org.

During the Product Shortage Period, Consider One or More of the Following Measures:

1. Assess each patient as to the indication for parenteral nutrition (PN) and provide nutrition via the oral or enteral route when possible.
2. Consider switching to oral or enterally administered electrolyte or mineral supplement products when oral/enteral intake is initiated (excluding patients with malabsorption syndromes or nonfunctioning gastrointestinal tract). Consult a pharmacist for product information.
3. Purchase only as much electrolyte and mineral injections supply as needed. In the interest of fair allocation to all patients nationally, please do not stockpile.
4. Reserve intravenous electrolyte and mineral products for those patients receiving PN or those with a therapeutic medical need for intravenous electrolytes and minerals.
5. Eliminate the use of parenteral electrolyte/mineral injections as a supplemental additive in enteral nutrition products.

6. Limit the use of electrolyte/mineral additives in IV fluids to patients with disease states and clinical conditions for which they are appropriate.
7. Reconsider the use of serum electrolyte algorithms/protocols as "automatic" IV electrolyte replacement therapies in otherwise asymptomatic patients.
8. Use commercially available IV multi-electrolyte/mineral products as much as possible for replacement therapy.
9. Review the entire portfolio of parenteral nutrition electrolyte and mineral products available nationally. There may be a shortage in one concentration or salt form but availability in another form. See Table 1 for alternative electrolyte and mineral salts.
10. Assess your PN patient population to determine if a **standardized, commercially available parenteral nutrition product with standard electrolytes**[1] might be appropriate for a portion of your patient population. Generally, additional components can be added to these products.
11. Assess your PN patient population to determine if a **standardized, commercially available multi-electrolyte product** might be appropriate for a portion of those patients.
12. During prolonged shortages of intravenous electrolytes and mineral products, the FDA may approve the temporary importation of alternative products. These products may have different salts, concentrations, packaging and labeling than United States approved products. The Dear Healthcare Professional Letter accompanying imported products should be read carefully.
13. Consider decreasing or eliminating the daily amount of electrolyte added to the PN.
14. Monitor serum electrolyte concentrations closely.
15. Observe for an increase in deficiencies with the ongoing shortages. Increase your awareness and assessment for signs and symptoms of electrolyte and mineral deficiencies.
16. Consider compounding PN in a single, central location (either in a centralized pharmacy or as outsourced preparation) in order to decrease inventory waste.
17. Facilities and practitioners need to continue to observe and be compliant with the product labeling (e.g., package insert), USP General Chapter <797> Pharmaceutical Compounding-Sterile Preparations, and state Boards of Pharmacy and federal rules and regulations.
18. Include PN component shortages and outages in the health care organization's strategies and procedures for managing medication shortages and outages.
19. Report severe drug product shortage information to the U.S. FDA Drug Shortage Program (DSP).
20. Report any patient problems related to shortages to ISMP Medication Errors Reporting Program (MERP).

Consider one or more of the following measures for managing each electrolyte and mineral shortage and their related signs and symptoms of deficiencies:

IV Concentrated Calcium Shortage

1. If calcium gluconate is removed from the PN formulation, monitor serum calcium concentrations and preferably ionized calcium concentrations.
2. If intravenous calcium is necessary, administer calcium chloride as a separate infusion from the PN. It is important to note the difference in the amount of elemental calcium provided by calcium chloride

as compared to the gluconate salt. Calcium chloride 1g provides 270 mg elemental calcium (13.6 mEq) and calcium gluconate 1 g provides 93mg elemental calcium (4.65 mEq).

3. Consider commercially available multi-electrolyte products that contain calcium for addition to PN. (Note these products may contain calcium as the chloride salt.)
4. Consider commercially available standardized PN products that contain calcium. (Note these products may contain calcium as the chloride salt.)
5. Calcium gluconate is the preferred form of calcium used in multicomponent PN. It is important to note that solubility curves for PN formulations containing calcium gluconate cannot be applied to calcium chloride. The quantitative amount of calcium to add as calcium chloride to a PN formulation that contains **inorganic** phosphate is VERY limited. The literature describing adding calcium chloride to PN formulations containing **inorganic** phosphate must be carefully reviewed and evaluated before making the decision to add calcium chloride to PN admixtures.[2-6] There is no published information on calcium phosphate solubility in a dextrose/amino acids/IV fat emulsion (total nutrient admixture) PN formulation using inorganic phosphate and calcium chloride.
6. Signs and symptoms of calcium deficiency: irritability, hyperventilation, tetany, other neuromuscular, CNS and cardiovascular symptoms.[7,8]

IV Concentrated Magnesium Shortage

1. Use premixed, intravenous magnesium products as much as possible for IV maintenance/ replacement therapy.
2. Minimize the use of IV magnesium additives in IV fluids.
3. Signs and symptoms of magnesium deficiency: ECG changes, arrhythmias, muscle spasms/tetany, nausea, lethargy, confusion, seizures, coma, and death.[7,8]

IV Concentrated Phosphate Shortage

1. Consider using the alternate salt IV phosphate as available and balance the sodium and potassium accordingly.
2. Consider oral or enteral phosphate products/supplements to replete or maintain serum phosphorus concentrations.
3. Consider commercially available standardized, commercial PN products that contain phosphate.
4. Decrease the daily amount/dose of phosphate added to PN formulations.
5. Reserve phosphates for pediatric and neonatal patients requiring PN.
6. Reserve phosphates for those patients with a therapeutic medical need for phosphorus.
7. Consider using IV organic phosphate injections, if available.
8. Consider provision of daily IV fat emulsion to all PN patients as clinically appropriate. Note: IV fat emulsions contain 15 mmol/L of phosphate as egg phospholipids.
9. Signs and symptoms of phosphorus deficiency: impaired diaphragmatic contractility, tachycardia, hypocapnia, respiratory failure, tissue hypoxia, decreased myocardial contractility, paralysis, weakness, paresthesias, neurologic dysfunction, seizures, death.[7,8]

IV Concentrated Potassium Shortage

1. Consider using alternate IV potassium salts as available and balance the chloride, acetate and phosphate accordingly.

2. Consider oral or enteral potassium products/supplements to replete or maintain serum potassium levels.
3. Use premixed, intravenous potassium products as much as possible for IV maintenance/ replacement therapy. Minimize the use of IV potassium additives in IV fluids.
4. Signs and symptoms of potassium deficiency: nausea, vomiting, weakness, muscle cramping, constipation, EKG changes, cardiac arrhythmias, sudden death, paralysis, respiratory compromise, and rhabdomyolysis.[7,8]

IV Concentrated Sodium Shortage:

1. Consider using alternate IV sodium salts and concentrations as available and balance the chloride, acetate and phosphate accordingly.
2. Consider administering IV medications in 0.9% sodium chloride (normal saline) instead of 5% dextrose in water (D5W) when compatible.
3. Consider changing/increasing the sodium concentration of IV fluids (0.45% to 0.9% sodium chloride).
4. Consider using 0.9% sodium chloride (normal saline) for irrigation with enteral nutrition when patients are on both enteral and parenteral therapy.
5. Signs and symptoms of sodium deficiency: headache, lethargy, disorientation, restlessness, nausea, vomiting, muscle cramps or weakness, depressed reflexes, seizures, coma, and death.[7,8]

Table 1. Electrolytes and Minerals Available/Alternative Salts

Electrolyte/Mineral	Available/Alternative Salts
Calcium	Gluconate* Chloride
Magnesium	Sulfate* Chloride
Phosphate	Potassium Sodium
Potassium	Acetate Chloride Phosphate
Sodium	Acetate Chloride Phosphate Bicarbonate** Lactate**

*Preferred salt for PN admixtures
**Avoid adding PN admixtures

References

1. ASPEN Board of Directors and Task Force on Parenteral Nutrition Standardization: Kochevar M, Guenter P, Holcombe B, Malone A, Mirtallo J. ASPEN statement on parenteral nutrition standardization. *JPEN J Parenter Enteral Nutr* 2007; 31(5):441–448.

2. Henry RS, et al. Compatibility of calcium chloride and calcium gluconate with sodium phosphate in a mixed TPN solution. *Am J Hosp Pharm*. 1980; 37:673-4.
3. Migaki EA, Melhart BJ, Dewar C, Hutson RK. Calcium chloride and sodium phosphate in neonatal parenteral nutrition containing TrophAmine: Precipitation and aluminum content. *JPEN J Parenter Enteral Nutr.* 2012;36:470-475.
4. Driscoll DF, Newton DW, Bistrian BR. Potential hazards of precipitation associated with calcium chloride in parenteral nutrition admixtures: Response to Migaki et al. *JPEN J Parenter Enteral Nutr.* 2012;36:497-498.
5. Hutson RK, Migaki EA. Issues concerning the safety of calcium chloride in neonatal parenteral nutrition: Response to the letter from Drs. Driscoll, Newton, and Bistrian. *JPEN J Parenter Enteral Nutr.* 2012;36:498-500.
6. Hutson RK, Christensen JM, Karnpracha C, et al. Calcium chloride in neonatal parenteral nutrition: Compatibility studies using laser methodology. PloS One. 9(9):e106825. Doi:10.1371/journal.pone.0106825.
7. Kraft M, et al. Treatment of electrolyte disorders in adult patients in the intensive care unit. *Am J Health-Syst Pharm.* 2005; 62:1663-82.
8. Rhoda KM, Porter MJ, Quintini C. Fluid and electrolyte management: putting a plan in motion. *JPEN J Parenter Enteral Nutr.* 2011; 35:375-685.

Suggested Readings

Canada TW, Tajchman SK, Tucker AM, Ybarra JV, eds. The ASPEN Fluids, Electrolytes, and Acid-Base Disorders Handbook. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition. 2015.

Kraft MD. Phosphorus and calcium: A review for the adult nutrition support clinician. Nutr Clin Pract. 2015; 30:21-33.

Langley G, Tajchman S. Fluids, electrolytes, and acid-base disorders. In: Mueller CM, ed. ASPEN Adult Nutrition Support Core Curriculum, 2nd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2012; 98-120.

Schmidt GL. Fluids and electrolytes. In: Corkins MR, ed. ASPEN Pediatric Nutrition Support Core Curriculum, 2nd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2015; 107-128.

About ASPEN

The American Society for Parenteral and Enteral Nutrition (ASPEN) is dedicated to improving patient care by advancing the science and practice of nutrition support therapy and metabolism. Founded in 1976, ASPEN is an interdisciplinary organization whose members are involved in the provision of clinical nutrition therapies, including parenteral and enteral nutrition. With members from around the world, ASPEN is a community of dietitians, nurses, nurse practitioners, pharmacists, physicians, PAs, researchers, scientists, and students from every facet of nutrition support clinical practice, research, and education. For more information about ASPEN, please visit www.nutritioncare.org.