2024 Parenteral Nutrition Product Shortage Recommendations: Intravenous Multivitamins

Updated October 9, 2024

The American Society for Parenteral and Enteral Nutrition (ASPEN) is a professional society of physicians, nurses, dietitians, pharmacists, other allied health professionals, and researchers. ASPEN envisions an environment in which every patient receives safe, efficacious, and high-quality patient care. ASPEN's mission is to improve patient care by advancing the science and practice of clinical nutrition and metabolism. ASPEN has developed parenteral nutrition (PN) shortage recommendations to assist its members and other clinicians in coping with PN shortages for their patients. These intravenous multivitamin product shortage recommendations were approved by the ASPEN Parenteral Nutrition Committee and the Board of Directors.

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I. General Recommendations for Intravenous Multivitamins Shortage Management

A. During an intravenous multivitamin shortage, ASPEN recommends consideration of the following general measures:
   1. For all patients, routinely assess and reassess patient-specific indication(s) for nutrition support and requirements for PN; provide nutrition, including multivitamins, via the oral or enteral route when possible and clinically appropriate.[1]
   2. **Do not stockpile**. In the interest of fair allocation to all patients, purchase only as much supply as needed.
   3. **Ensure understanding of differences among intravenous multivitamin products**. During prolonged shortages of intravenous multivitamin products, the FDA may approve the temporary importation of alternative products. These products may have different vitamin profiles, ratios (doses), packaging, and labeling than United States products. The Dear Healthcare Professional Letter accompanying imported products should be read carefully. Members of the healthcare team should be educated on any differences between imported products and products approved for use in the United States.
   4. **When enteral or oral multivitamins are used due to an intravenous multivitamin shortage, ensure the product contains a complete multivitamin profile**.
      a. Ensure the oral or enteral multivitamin product contains all vitamin components of the intravenous multivitamin product(s).
      b. Refer to Table 1 for the content of intravenous multivitamin products.

Table 1. Commercially available intravenous multivitamin products in the U.S.[2, 3]

VITAMIN	INFUVITE® ADULT (per 10 mL)*	INFUVITE® PEDIATRIC (per 5 mL)*
A (palmitate)	3300 units (1 mg)	2300 units (0.7 mg)
D (cholecalciferol)	200 units (5 mcg)	400 units (10 mcg)
E (dl-alpha tocopheryl acetate)	10 units (10 mg)	7 units (7 mg)
K (phytonadione)	150 mcg	200 mcg
C (ascorbic acid)	200 mg	80 mg
B-1 (thiamine)	6 mg	1.2 mg
B-2 (riboflavin)	3.6 mg	1.4 mg
B-3 (niacinamide)	40 mg	17 mg
B-5 (dexpanthenol)	15 mg	5 mg
B-6 (pyridoxine)	6 mg	1 mg
B-12 (cyanocobalamin)	5 mcg	1 mcg
B-7 (biotin)	60 mcg	20 mcg
B-9 (folic acid)	600 mcg	140 mcg
OTHER INGREDIENTS		
Aluminum*	less than or equal to 70 mcg/L	less than or equal to 30 mcg/L
Polysorbate 80 (only vial 1)	70 mg	50 mg
Propylene glycol (only vial 2)	1.5 g	None

***Combined vials 1 and 2**

Consult the manufacturer's product literature for a complete list of inactive ingredients. INFUVITE® ADULT MULTIPLE VITAMINS is indicated for adults and children aged 11 years and older.

5. **Maintain or incorporate the following sterile compounding practices:**
    a. Hospitals and alternate site facilities should use bulk package intravenous multivitamin products when available and reserve single-dose intravenous multivitamin products for patients receiving PN in the home setting.
    b. Compound PN in a single, central location (either in a centralized pharmacy or as outsourced preparation) to decrease inventory waste. Consider a supply outreach to other facilities in your geographic location.
    c. Facilities must continue to observe and comply 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.[2-4]
    d. The decision between adding individual vitamins to the PN admixture or administering separately from the PN should be based upon published or manufacturer-provided compatibility and stability data as well as compliance with standards for beyond-use dating of each pharmacy preparation.[4, 5]

* Note that commercially-produced intravenous multivitamins are supplied as two vials containing different vitamin profiles. Vials 1 and 2 are combined during preparation, resulting in a final product with a complete vitamin profile. **All dosing recommendations in this document refer to the final product volume once vials 1 and 2 have been combined.**[2, 3]

6. **Develop an organizational strategy.** Include PN component and product shortages in the healthcare organization's strategies and procedures for managing medication shortages. These procedures should include processes to:
    a. identify and monitor patients who are receiving a PN regimen that has been modified due to a product shortage,
    b. notify clinicians when a shortage of a PN component or product occurs,
    c. notify clinicians when PN formulations are adjusted due to shortages of PN components and products,
    d. notify patients receiving long-term (e.g., more than 1 month) PN therapy and their caregivers when their PN formulation has been adjusted for shortages of PN components and products,
    e. notify clinicians when a PN component shortage has resolved and
    f. **resume normal dosing practices when a PN component shortage has resolved (i.e., one full, age-appropriate dose of intravenous multivitamins in every PN admixture).**[2, 3] **It is critical to return to optimized dosing to prevent vitamin deficiencies, which may occur when patients are not receiving their full, age-appropriate doses of multivitamins with every PN admixture.**
7. **Report shortages and errors.**
    a. Report severe drug product shortage information to the FDA Center for Drug Evaluation and Research (CDER) Drug Shortage Program.
    b. Report any patient adverse events or medication hazards related to shortages to the ISMP Medication Errors Reporting Program (MERP).

II. Patient-Specific Recommendations for Intravenous Multivitamins Shortage Management

A. For **hospitalized neonatal and pediatric patients**, prioritize the supply of intravenous multivitamins as follows:
    1. Consider switching to oral or enterally administered multivitamins when oral/enteral intake meets greater than 50% of needs (excluding patients with severe malabsorption syndromes). Oral liquid, sublingual, chewable, or gummy multivitamins may not provide a complete vitamin profile. The vitamin profile should be reviewed. Any missing vitamin components should be provided, if available, to complement the incomplete multivitamin product. Note many oral liquid products contain sorbitol, which may cause diarrhea or gastrointestinal intolerance.
    2. Reserve pediatric intravenous multivitamins for children less than 2.5 kg or less than 36 weeks corrected gestational age.[6]
    3. Consider the use of adult intravenous multivitamins for children during a pediatric intravenous multivitamin shortage; use 5 mL of adult intravenous multivitamins in all children weighing greater than or equal to 2.5 kg or corrected gestational age of 36 weeks and older while saving the pediatric product for smaller neonates to conserve the supply.[6] The vitamin K content of the adult intravenous multivitamin product should be noted as it contains less vitamin K than the pediatric product. Provide additional vitamin K as appropriate to meet daily a total daily dose of 200 mcg. See Table 1 for ingredients in intravenous multivitamin products.[2, 3]
    4. If no pediatric intravenous multivitamins are available, infants less than 2.5 kg or less than 36 weeks corrected gestational age should receive an adult intravenous

multivitamin at a daily dose of 1 mL/kg up to a maximum of 2.5 mL/day.[6] The vitamin K content of the adult intravenous multivitamin product should be noted as it contains a lower dose of vitamin K than the pediatric product. Provide additional vitamin K as appropriate to meet a total daily dose appropriate for the patient's age and weight. See Table 1 for ingredients in intravenous multivitamin products.[2, 3]

5. When using adult intravenous multivitamin products in neonates, be aware that these products contain propylene glycol and greater amounts of polysorbate and aluminum, which may be toxic to neonates. Clinical judgment must prevail by weighing potential vitamin deficiencies against potential propylene glycol, polysorbate, and aluminum toxicity.
6. Use the standard dose (10 mL) of adult intravenous multivitamins for children aged 11 years and older, as the adult intravenous multivitamin product is approved for use in this population.[2, 3] (Please refer to the adult multivitamin recommendations in the event of a concurrent shortage.)
7. If neither pediatric nor adult intravenous multivitamins are available, administer individual intravenous vitamin entities in doses that are appropriate for the patient's age and weight. Components of an intravenous multivitamin that are available in an intravenous formulation include thiamine, folic acid, pyridoxine, ascorbic acid, and vitamin K.
    a. Renal excretion of water-soluble vitamins is increased with intravenous (vs. oral/enteral) administration, and higher plasma levels from rapid infusions of vitamins will also result in increased urinary excretion.[7, 8] Therefore, if IV vitamins are provided separately from the PN admixture, longer infusions should be used in preference, (i.e., 0.5 – 6 hours) should be used in preference over an IV push or short infusions (i.e., less than 0.5 hours). Considerations for each available IV vitamin are provided in Table 2.

B. For **alternate site and hospitalized adult patients**, prioritize the supply of intravenous multivitamins as follows:
    1. **The use of pediatric intravenous multivitamins for adults is not recommended. Using pediatric intravenous multivitamins for adults may contribute to a shortage of pediatric products. A shortage of pediatric intravenous multivitamins could create a potential risk of vitamin deficiencies in vulnerable neonatal and pediatric patients who may be more susceptible to vitamin deficiencies. Furthermore, pediatric intravenous multivitamins contain vitamins in doses or ratios that may be unsuitable for adults.[6]**
    2. Consider switching to oral or enterally administered multivitamins when oral/enteral intake is clinically appropriate (excluding patients with severe malabsorption syndromes). Oral liquid, sublingual, chewable, or gummy multivitamin products may not provide a complete vitamin profile. The vitamin profile should be reviewed. Any missing vitamin components should be provided, if available, to complement the incomplete multivitamin product. Note: many oral liquid medications contain sorbitol, which may cause diarrhea or gastrointestinal intolerance.
    3. Reserve intravenous multivitamins for those patients receiving solely PN for nutrition or those with a therapeutic medical need for intravenous multivitamins (e.g., severe malabsorption syndromes).
    4. When all options to obtain intravenous multivitamins have been exhausted, ration intravenous multivitamins in PN, such as reducing the daily dose by 50% or giving one multivitamin infusion dose (10 mL) three times a week.
    5. Patients who are not receiving their full, age-appropriate doses of multivitamins with every PN admixture due to product shortage should receive a complete formulation of an oral/enteral multivitamin DAILY unless they are strictly NPO or when enteral

administration is not appropriate. Some patients, such as those with malabsorption syndromes, may require supplementation with two doses of a complete oral/enteral multivitamin daily.

6. When all intravenous multivitamin products have been exhausted, consider the use of a commercially-produced intravenous vitamin B complex (thiamine 100mg, riboflavin 2mg, pyridoxine 2mg, dexpanthenol 2mg, niacinamide 100mg per 1 mL) and/or administration of individual intravenous vitamin entities.[9] Carefully evaluate daily intravenous vitamin intake from all sources. Components of an intravenous multivitamin that are available in an intravenous formulation include thiamine, folic acid, pyridoxine, ascorbic acid, and vitamin K.
    a. Renal excretion of water-soluble vitamins is increased with intravenous (vs. oral/enteral) administration, and higher plasma levels from rapid infusions of vitamins will also result in increased urinary excretion.[7, 8] Therefore, if IV vitamins are provided separately from the PN admixture, longer infusions (i.e., 0.5 – 6 hours) should be used in preference over an IV push or short infusions (i.e., less than 0.5 hours).
    b. Considerations for each available IV vitamin are provided in Table 2.

C. For **neonatal, pediatric and adult patients on PN at home**, prioritize the supply of intravenous multivitamin as follows:
    1. For neonatal and pediatric patients: refer to Section II. A. for recommendations.
    2. For adult patients:
        a. **The use of pediatric intravenous multivitamins for adults is not recommended. Using pediatric intravenous multivitamins for adults may contribute to a shortage of pediatric products. A shortage of pediatric intravenous multivitamins could create a potential risk of vitamin deficiencies in vulnerable neonatal and pediatric patients who may be more susceptible to vitamin deficiencies. Furthermore, pediatric intravenous multivitamins contain vitamins in doses or ratios that may be unsuitable for adults.[6]**
        b. Consider switching to oral or enterally administered multivitamins when oral/enteral intake is clinically appropriate (excluding patients with severe malabsorption syndromes). Oral liquid, sublingual, chewable or gummy multivitamin products may not provide a complete vitamin profile. The vitamin profile should be reviewed. Any missing vitamin components should be provided, if available, to complement the incomplete multivitamin product. Note: many oral liquid medications contain sorbitol, which may cause diarrhea or gastrointestinal intolerance.
    3. All efforts should be made to prioritize the supply of *single-dose* vials of intravenous multivitamins for patients in the home setting as utilizing pharmacy bulk vials of multivitamins in this setting is not feasible. Under normal circumstances, patients or caregivers in the home setting (rather than the sterile compounding pharmacy) prepare the intravenous multivitamins for addition to the PN admixture just prior to administration due to stability limitations of the multivitamin product. However, preparing doses of each individual vitamin from the vial for addition to the PN admixture as described in Table 2 may not be appropriate in the home setting.
        a. Some pharmacies may consider compounding syringes of age-appropriate doses of the individual vitamins listed in Table 2 for addition to the PN admixture at home. This should only be done when supporting compatibility and stability data are available.
    4. If a shortage requires the dose of intravenous multivitamins to be reduced, patients should receive one full dose at least three times weekly.

a. If supply allows during periods of rationing, priority should be given to maintain daily intravenous multivitamin dosing for neonatal and pediatric patients and patients of all ages with severe malabsorption syndromes or known or suspected vitamin depletion or deficiencies.

5. All patients receiving PN admixtures with less than one full dose of intravenous multivitamins due to a shortage should receive an appropriate dosage form of an oral/enteral complete multivitamin DAILY unless they are strictly NPO or when enteral administration is not appropriate. Some patients, such as those with malabsorption syndromes, may require supplementation with two doses of a complete oral/enteral multivitamin daily. Ideally, this should be provided by their infusion pharmacy to minimize the risk of patients obtaining an oral multivitamin that is not complete.[10]
6. All patients and caregivers should receive both verbal and written counseling from their infusion provider about changes to their intravenous multivitamin dose due to a shortage and the importance of compliance with an oral complete multivitamin during the shortage.[10]

Table 2. Considerations for individual IV vitamin additives when all intravenous multivitamin products have been exhausted [2, 3]

Vitamin	Dose (per day)				Signs of deficiency	Clinical considerations
	Adults	Children				
		< 1 kg	1 – 2.9 kg	≥ 3 kg		
Thiamine	6 mg	0.36 mg	0.78 mg	1.2 mg	• Altered mental status, ataxia, ophthalmoplegia, nystagmus, weakness, neuropathy, cardiac failure, acidosis[11-13]	• **Maintaining provision of thiamine supplementation is critical as several deaths have resulted from cardiac failure due to thiamine deficiency when patients on long-term PN did not receive vitamins for three to four weeks.** Patients receiving a high carbohydrate load are particularly susceptible to thiamine deficiency.[14-23]
Folic acid	600 mcg	42 mcg	91 mcg	140 mcg	• Anemia (megaloblastic or macrocytic), cheilosis, glossitis, neurologic and neuropsychiatric changes (neuropathy, paresthesia,	• Megaloblastic anemia secondary to folate deficiency has been reported in patients receiving PN who did not receive folate for 4-5 weeks.[25]

					ataxia, confusion, dementia)[11, 24]	
Pyridoxine	6 mg	0.3 mg	0.65 mg	1 mg	• Dermatitis, cheilitis, glossitis, angular stomatitis, microcytic anemia, neuropathies, encephalopathy, seizures[8, 24]	• Injectable pyridoxine is susceptible to proton exchange with other micronutrients and self-aggregation in the presence of certain electrolytes.[5]
Ascorbic acid	200 mg	24 mg	52 mg	80 mg	• Petechiae, bleeding gums, corkscrew hairs, delayed wound healing, leukocyte dysfunction[11]	• Available in a 25 g/50 mL single-use vial only (i.e., each vial contains 125 *adult* doses at 200 mg/dose).[26] o Use in PN admixtures by most hospitals and alternate care sites may be limited by high product cost and waste. • The stability of ascorbic acid in PN admixtures is highly variable and larger doses may be unstable.[5]
Vitamin K	150 mcg	60 mcg	130 mcg	200 mcg	• Bruising, prolonged bleeding time, elevated prothrombin time/INR, decreased bone density[11]	• Suggested dosing for *adults* is 0.5 – 1 mg/week if administration is separate from the PN admixture. • Available in both ampules and vials.[27, 28] o **Vials** of 1 mg (0.5 mL) should be reserved for patients requiring PN in the home setting. • Lipid injectable emulsion products contribute varying doses of vitamin K.[11, 29]

III. Monitoring

A. Increased awareness of signs and symptoms of vitamin deficiencies is required for all clinicians involved in the management of PN with reduced doses of intravenous multivitamin.[30]
B. If a vitamin deficiency is suspected and confirmatory testing is desired, clinicians should consider consulting their laboratory prior to testing for guidance on proper handling and storage of blood samples, as vitamin concentrations are particularly susceptible to degradation by several different environmental factors. If applicable, the effect of inflammation on serum concentrations of each micronutrient should be considered when interpreting laboratory results.[24, 31]

IV. ASPEN Resources for Intravenous Multivitamin Dosing

Webinar: "Optimizing Patient Care During a Multivitamin Shortage"—*Recorded March 4, 2021*
A recording of this free informational webinar on managing current intravenous multivitamin shortages across the age continuum and the safe use of temporarily imported multivitamins is available in the **ASPEN eLearning Center**.

Practice Tool: Dosing Multivitamins in PN Outside of a Shortage: Practicing the Standard of Care
A practice tool describing best practices for intravenous multivitamins outside of a shortage setting and the clinical implications of excluding intravenous vitamins from PN admixtures. Physical signs and symptoms of select vitamin deficiencies are also described. This document is available in ASPEN's **PN Resources**.

Important Note: These recommendations do not constitute medical or professional advice and should not be taken as such. To the extent the information published herein may be used to assist in the care of patients, this is the result of the sole professional judgment of the attending health professional whose judgment is the primary component of quality medical care. The information presented herein is not a substitute for the exercise of such judgment by the health professional.

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

References

1. Worthington P, Balint J, Bechtold M, et al. When Is Parenteral Nutrition Appropriate? *JPEN J Parenter Enteral Nutr*. 2017;41(3):324-377.
2. Infuvite Pediatric (multiple vitamins injection) [prescribing information]. Deerfield, IL: Baxter Healthcare Corporation; 2016.
3. Infuvite Adult (multiple vitamins injection) [prescribing information]. Deerfield, IL: Baxter Healthcare Corporation; 2016.
4. USP General Chapter <797> *Pharmaceutical Compounding- Sterile Preparations*. United States Pharmacopeial Convention. 2022. .
5. Boullata JI, Mirtallo JM, Sacks GS, et al. Parenteral nutrition compatibility and stability: A comprehensive review. *JPEN J Parenter Enteral Nutr*. 2022;46(2):273-299.
6. 2021 Parenteral Nutrition Multivitamin Product Shortage Considerations. American Society for Parenteral and Enteral Nutrition. Accessed July 29, 2024.

https://www.nutritioncare.org/Guidelines_and_Clinical_Resources/Product_Shortages/2021_Parenteral_Nutrition_Multivitamin_Product_Shortage_Considerations/.
7. Vanek VW, Borum P, Buchman A, et al. A.S.P.E.N. position paper: recommendations for changes in commercially available parenteral multivitamin and multi-trace element products. *Nutr Clin Pract*. 2012;27(4):440-491.
8. Sugandhi VV, Pangeni R, Vora LK, et al. Pharmacokinetics of vitamin dosage forms: A complete overview. *Food Sci Nutr*. 2024;12(1):48-83.
9. Vitamin B-Complex 100 Injection [prescribing information]. Morgantown, WV: Mylan Institutional LLC; 2021.
10. Mulherin DW, Kumpf V, Shingleton K. Managing nutrition support product shortages: What have we learned? *Nutr Clin Pract*. 2023;38(1):27-45.
11. McKeever L. Vitamins and trace elements. In: Mueller CM, Lord LM, Marian M, McClave SA, Miller SJ, eds. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:223-93.
12. Polegato BF, Pereira AG, Azevedo PS, et al. Role of Thiamin in Health and Disease. *Nutr Clin Pract*. 2019;34(4):558-564.
13. Kohnke S, Meek CL. Don't seek, don't find: The diagnostic challenge of Wernicke's encephalopathy. *Ann Clin Biochem*. 2021;58(1):38-46.
14. Blennow G. Wernicke encephalopathy following prolonged artificial nutrition. *Am J Dis Child*. 1975;129(12):1456.
15. Centers for Disease C. Deaths associated with thiamine-deficient total parenteral nutrition. *MMWR Morb Mortal Wkly Rep*. 1989;38(3):43-46.
16. Centers for Disease C, Prevention. Lactic acidosis traced to thiamine deficiency related to nationwide shortage of multivitamins for total parenteral nutrition -- United States, 1997. *MMWR Morb Mortal Wkly Rep*. 1997;46(23):523-528.
17. Chandrakumar A, Bhardwaj A, t Jong GW. Review of thiamine deficiency disorders: Wernicke encephalopathy and Korsakoff psychosis. *J Basic Clin Physiol Pharmacol*. 2018;30(2):153-162.
18. Hahn JS, Berquist W, Alcorn DM, et al. Wernicke encephalopathy and beriberi during total parenteral nutrition attributable to multivitamin infusion shortage. *Pediatrics*. 1998;101(1):E10.
19. Harper CG. Sudden, unexpected death and Wernicke's encephalopathy: a complication of prolonged intravenous feeding. *Aust N Z J Med*. 1980;10(2):230-235.
20. Kramer J, Goodwin JA. Wernicke's encephalopathy. Complication of intravenous hyperalimentation. *JAMA*. 1977;238(20):2176-2177.
21. Nadel AM, Burger PC. Wernicke encephalopathy following prolonged intravenous therapy. *JAMA*. 1976;235(22):2403-2405.
22. Ramsi M, Mowbray C, Hartman G, et al. Severe lactic acidosis and multiorgan failure due to thiamine deficiency during total parenteral nutrition. *BMJ Case Rep*. 2014;2014.
23. Velez RJ, Myers B, Guber MS. Severe acute metabolic acidosis (acute beriberi): an avoidable complication of total parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 1985;9(2):216-219.
24. Berger MM, Shenkin A, Schweinlin A, et al. ESPEN micronutrient guideline. *Clin Nutr*. 2022;41(6):1357-1424.
25. Denburg J, Bensen W, Ali MA, et al. Megaloblastic anemia in patients receiving total parenteral nutrition without folic acid or vitamin B12 supplementation. *Can Med Assoc J*. 1977;117(2):144-146.
26. ASCOR (ascorbic acid injection) [prescribing information]. Santa Ana, CA: McGuff Pharmaceuticals Inc; 2022.
27. Phytonadione injectable emulsion [prescribing information]. Warren, NJ: Cipla USA Inc; 2022.
28. Phytonadione injectable emulsion [prescribing information]. Lake Forest, IL: Hospira Inc; 2021.

29. Forchielli ML, Conti M, Motta R, et al. Phytonadione Content in Branded Intravenous Fat Emulsions. *JPEN J Parenter Enteral Nutr*. 2017;41(3):489-495.
30. Esper DH. Utilization of nutrition-focused physical assessment in identifying micronutrient deficiencies. *Nutr Clin Pract*. 2015;30(2):194-202.
31. Berger MM, Talwar D, Shenkin A. Pitfalls in the interpretation of blood tests used to assess and monitor micronutrient nutrition status. *Nutr Clin Pract*. 2023;38(1):56-69.