

May 28, 2015

## ASPEN Releases New Parenteral Nutrition L-Cysteine Product Shortage Considerations

ASPEN has developed parenteral nutrition (PN) shortage considerations to assist its members and other clinicians in coping with PN shortages in their patients.

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

- [American Society of Health-System Pharmacists \(ASHP\), Drug Shortages Resource Center](#)
- [U.S. FDA Drug Shortages](#)
- [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](mailto:clinicalpractice@nutritioncare.org).

Cysteine is an amino acid which is important in the synthesis of proteins and has a role in growth and the production of antioxidants. It is considered a conditionally essential amino acid in preterm infants due to the biochemical immaturity of the enzyme cystathionase, which converts methionine to cysteine and ultimately to taurine. An additional consideration for the addition of L-cysteine as the hydrochloride (HCl) salt to PN admixtures is for further acidification of the admixture thus improving calcium and phosphorus, as phosphate, solubility. Every 160 mg of L-cysteine delivers 1 mmole HCl. While there is no replacement for L-cysteine, dose conservation measures can be taken.

### During the L-cysteine shortage period, consider one or more of the following measures:

1. Assess each patient as to the indication for PN and provide nutrition via the oral or enteral route when possible.
2. Discontinue L-cysteine supplementation in PN for neonates receiving a minimum dose of 3 g/kg per day of commonly-prescribed amino acids solutions. This dose of amino acids will provide sufficient amount of sulfur amino acid substrate (methionine) for the transsulfuration pathway to produce

adequate cysteine and thus no need to supplement parenteral nutrition (PN) with L-cysteine. However, L-cysteine supplementation may be necessary to decrease the pH of the PN admixture in order to enhance calcium and phosphate solubility.

3. Reduce L-cysteine supplementation in PN formulations to 20 mg per gram of amino acids provided. Common dosing of L-cysteine in PN formulations is 30-40 mg per gram of amino acids provided. However, studies have documented that as little as 20 mg per gram of amino acids is adequate.
4. Assess the PN formulation to determine if the daily calcium and phosphorus requirements are considered compatible and within solubility limits and can be attained without the addition of L-cysteine.
5. When removing or reducing the dose of L-cysteine in the PN formulation re-evaluate the calcium-phosphorus solubility charts or software to insure that a precipitate will not develop due to the increase in the pH of the PN admixture. Consider using calcium-phosphorus solubility data that do not include the presence of L-cysteine in the PN formulation.
6. Consider using organic phosphate injections, if available. Organic phosphates, as compared to inorganic phosphorus products, have favorable compatibility with calcium and may be considered as a measure to provide adequate calcium and phosphate to patients with decreased risk of precipitate formation.
7. Discourage using L-cysteine as an agent to re-establish vascular access device catheter patency.
8. Purchase only as much L-cysteine injections supply as needed. In the interest of fair allocation to all patients nationally, please do not stockpile.
9. Compound PN in a single, central location (either in a centralized pharmacy or as outsourced preparation) in order to decrease inventory waste. Consider a supply outreach to other facilities in your geographic location.
10. If using an automated compounding device (ACD) to prepare PN formulations add the L-cysteine to the PN as a separate additive rather than adding it to the amino acid solution (so that it is pumped as a single component). This will conserve supplies and reserve its use for the intended population. Consult the ACD manufacturer for proper placement of L-cysteine on the ACD configuration. For manual compounding, add the L-cysteine to the PN immediately before or after adding the amino acids solution and prior to adding the calcium.
11. Facilities and practitioners must 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.
12. Report severe drug product shortage information to the [FDA Drug Shortage Program \(DSP\)](#).
13. Report any patient problems related to shortages to [ISMP Medication Errors Reporting Program \(MERP\)](#).

### Suggested Readings:

1. Riedijk MA, van Beek RHT, Voortman G, de Bie HMA, Dassel ACM, van Goudoever JB. Cysteine: a conditionally essential amino acid in low-birth-weight preterm infants? *Am J Clin Nutr.* 2007; 86:1120-1125.
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12. Sturman JA, Gaull G, Raiha NCR. Absence of cystathionase in human fetal liver: Is cystine essential? *Science* . 1970;169:74–76.
13. Zlotkin SH, Anderson GH. Sulfur balances in intravenously fed infants: effects of cysteine supplementation. *Am J Clin Nutr* . 1982;36:862–867.
14. Lyons J, Rauh-Pfeiffer A, Ming-Yu Y, et al. Cysteine metabolism and whole blood glutathione synthesis in septic pediatric patients. *Crit Care Med*. 2001;29(4):870–877.

## 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](http://www.nutritioncare.org).