

November 4, 2019

Parenteral Nutrition (PN) products: light protection required to reduce the risk of serious adverse effects in premature neonates

Dear Healthcare Professional,

Fresenius Kabi seeks to inform you of recent recommendations from the European Medicines Agency regarding all parenteral nutrition products containing amino acids and/or lipids, indicated for use in neonates and in children below 2 years and the following new safety information:

Summary

- **During administration to neonates and children below 2 years of age, parenteral nutrition products containing amino acids and/or lipids, should be protected from light (containers and administration sets).**
- **Use of light-exposed parenteral nutrition products containing amino acids and/or lipids, particularly in admixtures with vitamins and/or trace elements, may lead to severe adverse effects in premature neonates. This is because exposure of such solutions to light causes formation of peroxides and other degradation products.**
- **Premature neonates are considered at high risk of oxidative stress related to multiple risk factors including oxygen therapy, phototherapy, weak immune system and inflammatory response with reduced oxidant defense.**

Background on the Safety Concern

Data in support of this effect from light exposure include studies showing that the formation of PN photodegradation products can be slowed down or prevented by the application of various light protection measures². A meta-analysis of four randomized controlled trials suggests a reduced mortality at 36 weeks' gestational age when light protection is in place (Chessex et al, 2017)².

1. Ayers P, Adams S, Boullata JI, et al. ASPEN parenteral nutrition safety consensus recommendations. JPEN J Parenter Enteral Nutr 2014;38(3):296-333 and Worthington P, Balint J, Bechtold M, et al. When is parenteral nutrition appropriate? JPEN J Parenter Enteral Nutr 2017;41(3):324-377.

2. Chessex, S. Laborle, N. Nasef, et al. Shielding Parenteral Nutrition From Light Improves Survival Rate in Premature Infants. JPEN J Parenter Enteral Nutr 2017; 41(3): 378-383.

The clinical relevance of light protection of PN products is especially notable in premature infants with high nutritional requirements and slow intravenous infusion rates.

PN containing vitamins and/or lipids may be most susceptible. Ambient and environmental light and especially phototherapy contribute to generation of peroxides.

Fresenius Kabi's parenteral nutritional (PN) products approved in the U.S. include the following:

- Omegaven® (fish oil triglycerides) injectable emulsion is indicated for use in pediatric patients with PNAC (parenteral nutrition associated cholestasis).
- Smoflipid® (lipid injectable emulsion), USP 20% is indicated for use in adults only. Safety and efficacy in pediatrics have not been established.
- Kabiven® (amino acids, electrolytes, dextrose and lipid injectable emulsion) is indicated for use in adults only. Safety and efficacy in pediatrics have not been established.
- Intralipid® (lipid injectable emulsion) is indicated for use in adults and pediatric patients³

Call for reporting

Healthcare professionals should report suspected adverse drug reactions (ADRs) in neonates and children below 2 years of age treated with PN products per the below contact information. When reporting please provide as much information as possible.

For **medical inquiries**, contact:

Fresenius Kabi USA, LLC Medical Affairs, Clinical Nutrition

Toll Free: (800) 551-7176 (option 4)

E-mail: nutrition.medinfo.USA@fresenius-kabi.com

Fax: (847) 550-0207

To report **SUSPECTED ADVERSE REACTIONS**, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or email at: adverse.events.USA@fresenius-kabi.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Note: This letter is for scientific exchange purposes only and is not intended to be promotional. As set forth above, Smoflipid® and Kabiven® are indicated for use in adults only.

Fresenius Kabi, USA LLC

³ Intralipid® (lipid injectable emulsion) is manufactured by Fresenius Kabi for Baxter Healthcare Corporation.