FRESENIUS KABI

Admixture Stability Reference Guide

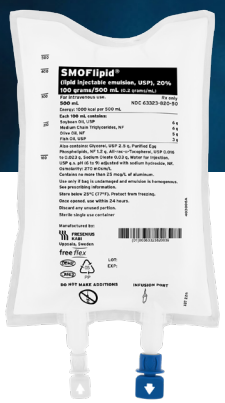
Pediatrics

The data presented within was obtained from the Medical Affairs Department at Fresenius Kabi USA.

How to use this guide:

- Admixture tables are ordered from the lowest concentration of SMOFlipid® or Omegaven® to the highest concentration and show the final concentrations of the tested admixtures.
- The formulations were tested with the maximum electrolyte content in the additives table and were found to be physically stable. A variety of formulations were tested. Only those formulations that were stable are included in this reference guide. Please contact Fresenius Kabi Medical Affairs Department for any unstable admixtures.
- Each formulation represents the minimum concentration required of each individual macronutrient to ensure stability. For example, for an admixture to be stable with a final concentration of SMOFlipid 2.1%, the final concentration of TrophAmine® must be at least 2.9% and the final concentration of dextrose must be at least 17.2%.
- SMOFlipid- and Omegaven-containing parenteral nutrition (PN) admixtures with TrophAmine 10% and Omegaven-containing PN admixtures with Premasol 10% have an 11-day stability (9 days refrigerated at 2°C to 8°C [36° to 46°F] followed by 48 hours at room temperature from 20°C to 25°C [68° to 77°F]). SMOFlipid-containing PN admixtures with Premasol 10% have a 10-day stability (9 days refrigerated at 2°C to 8°C [36°F to 46°F] followed by 24 hours at room temperature from 20°C to 25°C [68°F to 77°F]).
- Admixture stability with SMOFlipid and Omegaven was tested by visual inspection, pH, lipid globule size distribution, and mean lipid droplet diameter in compliance with USP ‹729› standards. No microbiological or chemical tests were conducted. Results are only valid for the branded products listed at the time of testing.
- Additions to the PN admixtures should be evaluated by a pharmacist for compatibility. If it is deemed advisable to introduce additives, use strict aseptic techniques to avoid microbial contamination.
- For detailed information on the data presented in this guide, please contact the Fresenius Kabi Medical Affairs Department at 1-800-551-7176 (option 4).

This guide is intended for admixture stability purposes only.
Clinical decisions regarding additions are the responsibility of the relevant healthcare provider.



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SMOFlipid®
(lipid injectable emulsion),
for intravenous use

Pediatric Amino Acids

Admixtures tested with **SMOFlipid** and **TrophAmine®** 10%, macronutrient final concentrations (%)

11-day admixture stability (9 days refrigerated followed by 48 hours at room temperature)

Admixtures[a]			
SMOFlipid 20%	2.1%	3.2%	3.6%
TrophAmine 10%	2.9%	4.3%	4.8%
Dextrose 70%	17.2%	21.6%	10.3%
Volume (mL)	280	280	250
Micronutrients			
Sodium chloride (mEq/kg/day)	5	2	2
Potassium acetate (mEq/kg/day)	4	2	2
Calcium gluconate (mEq/kg/day)	8	2	2
Magnesium sulfate (mEq/kg/day)	0.5	0.3	0.3
Sodium phosphate (mmol/kg/day)	2	1	1
INFUVITE® PEDiatric (mL/day) (Baxter)	3.25	3.25	3.25
Selenium (selenious acid) (mcg/kg/day) (American Regent®)	2	2	2
Zinc sulfate (mcg/kg/day) (American Regent)	400	250	250
Copper (cupric chloride) (mcg/kg/day) (Hospira)	20	20	20
Chromium (chromic chloride) (mcg/kg/day) (Hospira)	0.3	0.2	0.2
Manganese sulfate (mcg/kg/day) (American Regent)	1	1	1
Cysteine hydrochloride[b] (mg/kg/day) (Exela® Pharma Sciences)	160	0	0

[a] SMOFlipid admixture 2.1% concentration was based on a 2-kg infant; SMOFlipid admixtures 3.2% and 3.6% concentrations were based on a 3-kg infant.
[b] Cysteine was only added to SMOFlipid admixture 2.1% concentration; only evaluated in admixture based on a 2-kg infant.

Any significant change in pH from additives not listed compared to what has been evaluated in this study may affect compatibility.

Bringing more **options** to parenteral nutrition (PN)

Admixtures tested with **SMOFlipid®** and **Premasol** 10%, macronutrient final concentrations (%)

10-day admixture stability (9 days refrigerated followed by 24 hours at room temperature)

Admixtures[a]			
SMOFlipid 20%	2.3%	3%	3.2%
Premasol 10%	3%	3%	4.3%
Dextrose 70%	10.9%	25%	21.6%
Volume (mL)	200	360	280
Micronutrients			
Sodium chloride 23.4% (mEq/kg/day)	2	5	2
Potassium acetate (mEq/kg/day)	2	4	2
Calcium gluconate 10% (mEq/kg/day)	2	4	2
Magnesium sulfate 50% (mEq/kg/day)	0.3	0.5	0.3
Sodium phosphate (mmol/kg/day)	1	2	1
INFUVITE® PEDiatric (mL/day) (Vial 1 and Vial 2) (Baxter)	3.25	5	3.25
Multitrace-4® Neonatal[b] (Trace Elements) (mL/day) (American Regent®)	0.3	0.4	0.6

[a] SMOFlipid admixture 2.3% concentration was based on a 1.5-kg infant; SMOFlipid admixture 3% concentration was based on a 3.6-kg infant; SMOFlipid admixture 3.2% concentration was based on a 3-kg infant.
[b] Multitrace-4 Neonatal: Each 1 mL contains zinc (1.5 mg), copper (0.1 mg), manganese (25 mcg), and chromium (0.85 mcg).

Any significant change in pH from additives not listed compared to what has been evaluated in this study may affect compatibility.

Per the SMOFlipid Prescribing Information: Infuse admixtures containing SMOFlipid immediately. Infusion must be complete within 24 hours after removal from refrigeration. Discard any remaining admixture.

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Omegaven®
(fish oil triglycerides) injectable emulsion, for intravenous use

Pediatric Amino Acids

Admixtures tested with **Omegaven** and **TrophAmine®** 10%, macronutrient final concentrations (%)

11-day admixture stability (9 days refrigerated followed by 48 hours at room temperature)

Admixtures													
Omegaven 10%	0.4%	0.7%	0.7%	0.8%	0.8%	0.9%	1%	1%	1.1%	1.2%	1.3%	1.4%	1.9%
TrophAmine 10%	0.8%	1.4%	2.9%	2.4%	3%	2.7%	1%	3%	4.3%	4.8%	3.2%	2.7%	3.2%
Dextrose 70%	5.8%	12.5%	17.2%	6.9%	10.9%	16.8%	8.6%	25%	21.6%	10.3%	14.6%	16.8%	14.6%
Volume (mL)	1000	500	280	250	200	500	250	360	280	250	300	500	300

Electrolytes and additives in **Omegaven**-containing PN admixtures with **TrophAmine** 10%

Micronutrients	Range (weight-based dosing based on a 1.5 - 4.5 kg infant)
Sodium chloride	2 - 5 mEq/kg
Potassium acetate	2 - 4 mEq/kg
Calcium gluconate	2 - 4 mEq/kg
Magnesium sulfate	0.3 - 0.5 mEq/kg
(Inorganic) sodium phosphate	1 - 2 mmol/kg Phos (1.33 - 2.66 mEq/kg Na)
INFUVITE® PEDiatric (Vial 1 and Vial 2) (Baxter)	3.25 - 5 mL
Selenium (selenious acid) (American Regent®)	2 mcg/kg
Zinc sulfate (American Regent)	250 - 400 mcg/kg
Copper (cupric chloride) (Hospira)	20 mcg/kg
Chromium (chromic chloride) (Hospira)	0.2 - 0.3 mcg/kg
Manganese sulfate (American Regent)	1 mcg/kg
Cysteine hydrochloride[a] (Exela® Pharma Sciences)	0 - 160 mg/kg

[a] Cysteine was only added to Omegaven admixture 0.7% concentration with TrophAmine 10%; only evaluated in admixture based on a 2-kg infant.

Any significant change in pH from additives not listed compared to what has been evaluated in this study may affect compatibility.

Bringing more **choices** to parenteral nutrition (PN)

Admixtures tested with **Omegaven®** and **Premasol** 10%, macronutrient final concentrations (%)

11-day admixture stability (9 days refrigerated followed by 48 hours at room temperature)

Admixtures[a]							
Omegaven 10%	0.7%	0.8%	0.8%	0.9%	1%	1%	1.4%
Premasol 10%	2.9%	2.4%	3%	2.7%	1%	3%	2.7%
Dextrose 70%	17.2%	6.9%	10.9%	16.8%	8.6%	25%	16.8%
Volume (mL)	280	250	200	500	250	360	500
Micronutrients							
Sodium chloride (mEq/kg/day)	5	5	2	5	2	5	5
Potassium acetate (mEq/kg/day)	4	4	2	4	2	4	4
Calcium gluconate (mEq/kg/day)	8	4	2	4	2	4	4
Magnesium sulfate (mEq/kg/day)	0.5	0.5	0.3	0.5	0.3	0.5	0.5
Sodium phosphate (mmol/kg/day)	2	2	1	2	1	2	2
INFUVITE® PEDiatric (mL/day) (Baxter)	3.25	3.25	3.25	3.25	3.25	5	3.25
Selenium (selenious acid) (mcg/kg/day) (American Regent®)	2	2	2	2	2	2	2
Zinc sulfate (mcg/kg/day) (American Regent)	400	400	400	250	400	250	250
Copper (cupric chloride) (mcg/kg/day) (Hospira)	20	20	20	20	20	20	20
Chromium (chromic chloride) (mcg/kg/day) (Hospira)	0.3	0.3	0.3	0.2	0.3	0.2	0.2
Manganese sulfate (mcg/kg/day) (American Regent)	1	1	1	1	1	1	1
Cysteine hydrochloride[b] (mg/kg/day) (Exela® Pharma Sciences)	160	0	0	0	0	0	0

[a] Formulations based on infants weighing 2 kg (Omegaven admixture 0.7% concentration and Omegaven admixture 0.8% concentration/Premasol 2.4% concentration), 1.5 kg (Omegaven admixture 0.8% concentration/Premasol 3% concentration), 4.5 kg (Omegaven admixtures 0.9% and 1.4% concentrations), 2.5 kg (Omegaven admixture 1% concentration/Premasol 1% concentration), and 3.6 kg (Omegaven admixture 1% concentration/Premasol 3% concentration) in the admixture table above.

[b] Cysteine only added to Omegaven admixture 0.7% concentration; only evaluated in admixture based on a 2-kg infant.

Any significant change in pH from additives not listed compared to what has been evaluated in this study may affect compatibility.

Per the Omegaven Prescribing Information: Start the infusion of admixtures containing Omegaven immediately. If not used immediately, admixtures may be stored for up to 6 hours at room temperature or up to 24 hours under refrigeration. Complete the infusion within 24 hours after removal from storage. Any remaining contents of a partly used PN container must be discarded. Follow the instructions of each product included in the admixture.

INDICATIONS AND USAGE

SMOFlipid is indicated in adult and pediatric patients, including term and preterm neonates, as a source of calories and essential fatty acids for parenteral nutrition (PN) when oral or enteral nutrition is not possible, insufficient, or contraindicated.

IMPORTANT SAFETY INFORMATION

For intravenous infusion only into a central or peripheral vein. Use a non-vented non-DEHP 1.2 micron in-line filter set during administration. Recommended dosage depends on age, energy expenditure, clinical status, body weight, tolerance, ability to metabolize and eliminate lipids, and consideration of additional energy given to the patient. The recommended dose for adults and pediatrics is shown in Table 1. For information on age-appropriate infusion rate, see the full prescribing information. SMOFlipid Pharmacy Bulk Package is only indicated for use in pharmacy admixture programs for the preparation of three-in-one or total nutrition admixtures. Protect the admixed PN solution from light.

Table 1: Recommended Adult and Pediatric Dosage

Age	Nutritional Requirements	
	Initial Recommended Dosage	Maximum Dosage
Birth to 2 years of age (including preterm and term neonates)	0.5 to 1 g/kg/day	3 g/kg/day
Pediatric patients 2 to <12 years of age	1 to 2 g/kg/day	3 g/kg/day
Pediatric patients 12 to 17 years of age	1 g/kg/day	2.5 g/kg/day
Adults	1 to 2 g/kg/day	2.5 g/kg/day

SMOFlipid is contraindicated in patients with known hypersensitivity to fish, egg, soybean, peanut, or any of the active or inactive ingredients, and severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglycerides >1,000 mg/dL).

Clinical Decompensation with Rapid Infusion of Intravenous Lipid Emulsion in Neonates and Infants: Acute respiratory distress, metabolic acidosis, and death after rapid infusion of intravenous lipid emulsions have been reported.

Parenteral Nutrition-Associated Liver Disease: Increased risk in patients who received parenteral nutrition for greater than 2 weeks, especially preterm neonates. Monitor liver tests; if abnormalities occur, consider discontinuation or dosage reduction.

Hypersensitivity Reactions: Monitor for signs or symptoms. Discontinue infusion if reactions occur.

Risk of Infections, Fat Overload Syndrome, Refeeding Syndrome, Hypertriglyceridemia, and Essential Fatty Acid Deficiency: Monitor for signs and symptoms; monitor laboratory parameters.

Aluminum Toxicity: Increased risk in patients with renal impairment, including preterm neonates.

Most common adverse drug reactions (≥5%) from clinical trials in adults were nausea, vomiting, and hyperglycemia. Most common adverse drug reactions (≥5%) from clinical trials in pediatric patients were anemia, vomiting, increased gamma-glutamyltransferase, and nosocomial infection.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This Important Safety Information does not include all the information needed to use SMOFlipid safely and effectively. Please see full prescribing information for SMOFlipid (lipid injectable emulsion), for intravenous use at www.FreseniusKabiNutrition.com/SMOFlipidPI.

INDICATIONS AND USAGE

Omegaven is indicated as a source of calories and fatty acids in pediatric patients with parenteral nutrition-associated cholestasis (PNAC).

Limitations of Use

Omegaven is not indicated for the prevention of PNAC. It has not been demonstrated that Omegaven prevents PNAC in parenteral nutrition (PN)-dependent patients.

It has not been demonstrated that the clinical outcomes observed in patients treated with Omegaven are a result of the omega-6:omega-3 fatty acid ratio of the product.

IMPORTANT SAFETY INFORMATION

Protect the admixed PN solution from light. Prior to administration, correct severe fluid and electrolyte disorders and measure serum triglycerides to establish a baseline level. Initiate dosing in PN-dependent pediatric patients as soon as direct or conjugated bilirubin levels are 2 mg/dL or greater. The recommended nutritional requirements of fat and recommended dosages of Omegaven to meet those requirements for pediatric patients are provided in Table 1, along with recommendations for the initial and maximum infusion rates. Administer Omegaven until direct or conjugated bilirubin levels are less than 2 mg/dL or until the patient no longer requires PN.

Table 1: Recommended Pediatric Dosage and Infusion Rate

Nutritional Requirements	Direct Infusion Rate	
Recommended Initial Dosage and Maximum Dosage	Initial	Maximum
1 g/kg/day; this is also the maximum daily dose	0.2 mL/kg/hour for the first 15 to 30 minutes; gradually increase to the required rate after 30 minutes	1.5 mL/kg/hour

Omegaven is contraindicated in patients with known hypersensitivity to fish or egg protein or to any of the active ingredients or excipients, severe hemorrhagic disorders due to a potential effect on platelet aggregation, severe hyperlipidemia, or severe disorders of lipid metabolism characterized by hypertriglyceridemia (serum triglyceride concentrations greater than 1,000 mg/dL).

Clinical Decompensation with Rapid Infusion of Lipid Injectable Emulsions in Neonates and Infants: Acute respiratory distress, metabolic acidosis, and death after rapid infusion of intravenous lipid emulsions have been reported. Hypertriglyceridemia was commonly reported. Strictly adhere to the recommended total daily dosage; the hourly infusion rate should not exceed 1.5 mL/kg/hour. Carefully monitor the infant's ability to eliminate the infused lipids from the circulation (e.g., measure serum triglycerides and/or plasma free fatty acid levels). If signs of poor clearance of lipids from the circulation occur, stop the infusion and initiate a medical evaluation.

Hypersensitivity Reactions: Monitor for signs or symptoms. Discontinue infusion if reaction occurs.

Infections, Fat Overload Syndrome, Refeeding Syndrome, and Hypertriglyceridemia: Monitor for signs and symptoms; monitor laboratory parameters.

Aluminum Toxicity: Increased risk in patients with renal impairment, including preterm infants.

Monitoring and Laboratory Tests: Routine laboratory monitoring is recommended, including monitoring for essential fatty acid deficiency.

The most common adverse drug reactions (>15%) are vomiting, agitation, bradycardia, apnea, and viral infection.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This Important Safety Information does not include all the information needed to use Omegaven safely and effectively. Please see full prescribing information for Omegaven (fish oil triglycerides) injectable emulsion, for intravenous use at www.FreseniusKabiNutrition/OmegavenPI.

If you have any questions, please contact the Medical Affairs Department at 1-800-551-7176 (option 4) or email Nutrition.MedInfo.USA@fresenius-kabi.com

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