

Compatibility Reference Guide

TESTING METHODS

- Admixture stability with SMOfIipid was tested by visual inspection, pH, large-diameter lipid globule size distribution (PFAT5) 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.

SMOfIipid® Lipid Injectable Emulsion, USP 20%		Aminosyn® II 15% Amino Acid Injection	Plenamaine™ 15% Amino Acids Injection	Clinisol 15% Amino Acid Injection	ProSol 20% Amino Acid Injection	Travasol 10% Amino Acid Injection
Macronutrients ^a	Amino Acid Solution (g/L)	32-91	32-91	33-91	35-111	28-67
	SMOfIipid 20% (g/L)	12-67	12-67	12-67	14-74	9-56
	Dextrose 70% (g/L)	88-342	88-342	88-343	103-371	68- 297
Trace Elements & Adult Multivitamins	Infuvite Adult Injection (Baxter)	0 to 10 mL	0 to 10 mL	0 to 10 mL	0 to 10 mL	0 to 10 mL
	Addamel N ^b (Fresenius Kabi)	0 to 10 mL	0 to 10 mL	0 to 10 mL	0 to 10 mL	0 to 10 mL
Electrolytes ^c	Sodium	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L
	Potassium	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L
	Calcium	0 to 15 mEq/L	0 to 15 mEq/L	0 to 15 mEq/L	0 to 15 mEq/L	0 to 15 mEq/L
	Magnesium	0 to 15 mEq/L	0 to 15 mEq/L	0 to 15 mEq/L	0 to 15 mEq/L	0 to 15 mEq/L
	Chloride	0 to 300 mEq/L	0 to 300 mEq/L	0 to 300 mEq/L	0 to 300 mEq/L	0 to 300 mEq/L
	Acetate	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L	0 to 150 mEq/L
	(Inorganic) Phosphate ^d	0 to 15 mmol/L	0 to 15 mmol/L	0 to 15 mmol/L	0 to 15 mmol/L	0 to 15 mmol/L
Extended Stability		9 days total storage: 7 days storage at 2°-8°C, then 2 days at 20°-25°C.	9 days total storage: 7 days storage at 2°-8°C, then 2 days at 20°-25°C.	8 days total storage: 7 days storage at 2°-8°C, then 1 day at 20°-25°C.	8 days total storage: 7 days storage at 2°-8°C, then 1 day at 20°-25°C.	8 days total storage: 7 days storage at 2°-8°C, then 1 day at 20°-25°C.

^aThe range does not necessarily reflect the minimum concentration of each macronutrient to ensure stability.

^bAddamel N (for adults) is not FDA-approved for use in the U.S. Per 10 mL, it contains: iron (11 mg), zinc (6.5 mg), copper (1.26 mg), chromium (0.01 mg), fluoride (0.95 mg), and molybdenum (0.019 mg).

^cThe electrolyte salts used were sodium chloride, potassium acetate, calcium chloride, magnesium sulfate, and sodium phosphates. Any significant change in additions to the admixture compared to what has been evaluated in this study may affect stability/compatibility.

^dThe same limits are valid when additions of organic phosphate, sodium glycerophosphate (Glycophos) are used. Glycophos is not FDA-approved for use in the U.S.

ADDITIVES & STORAGE

- 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.
- Infuse admixtures containing SMOfIipid immediately. Infusion must be complete within 24 hours after removal from refrigeration. Discard any remaining admixture.

Contact us for specific extended stability information or any other questions pertaining to SMOfIipid All-in-One PN admixtures: (800) 551-7176 (Option #4) or by e-mail at: nutrition.medinfo.USA@fresenius-kabi.com.

WARNING: DEATH IN PRETERM INFANTS

- Deaths in preterm infants after infusion of intravenous lipid emulsions have been reported in the medical literature.
- Autopsy findings included intravascular fat accumulation in the lungs.
- Preterm infants and low-birthweight infants have poor clearance of intravenous lipid emulsion and increased free fatty acid plasma levels following lipid emulsion infusion.

SMOFLIPID (lipid injectable emulsion), for intravenous use

BRIEF SUMMARY OF PRESCRIBING INFORMATION FOR HEALTHCARE PROVIDERS

This brief summary does not include all the information needed to use SMOFLIPID safely and effectively. Please see full prescribing information, including Boxed Warning for SMOFLIPID (lipid injectable emulsion), for intravenous use at www.freseniuskabinutrition.com.

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INDICATIONS AND USAGE

SMOFLIPID is indicated in adults as a source of calories and essential fatty acids for parenteral nutrition (PN) when oral or enteral nutrition is not possible, insufficient, or contraindicated.

Limitations of Use

The omega-6: omega-3 fatty acid ratio and Medium Chain Triglycerides in SMOFLIPID have not been shown to improve clinical outcomes compared to other intravenous lipid emulsions.

DOSAGE AND ADMINISTRATION

The recommended daily dosage in adults is 1 to 2 grams/kg per day and should not exceed 2.5 grams/kg per day. SMOFLIPID 1000 mL is supplied as a Pharmacy Bulk Package for admixing only and is not for direct infusion. Prior to administration, transfer to a separate PN container. Protect the admixed PN solution from light.

CONTRAINDICATIONS

Known hypersensitivity to fish, egg, soybean, or peanut protein, or to any of the active ingredients or excipients.

Severe hyperlipidemia or severe disorders of lipid metabolism with serum triglycerides > 1,000 mg/dL.

WARNINGS AND PRECAUTIONS

- Death in Preterm Infants: (see BLACK BOX WARNING)
- Hypersensitivity Reactions: SMOFLIPID contains soybean oil, fish oil, and egg phospholipids, which may cause hypersensitivity reactions. Cross reactions have been observed between soybean and peanut oil. Signs or symptoms of a hypersensitivity reaction may include: tachypnea, dyspnea, hypoxia, bronchospasm, tachycardia, hypotension, cyanosis, vomiting, nausea, headache, sweating, dizziness, altered mentation, flushing, rash, urticaria, erythema, pyrexia, or chills. If a hypersensitivity reaction occurs, stop infusion of SMOFLIPID immediately and undertake appropriate treatment and supportive measures.
- Risk of Catheter-Related Infections: Lipid emulsions, such as SMOFLIPID, can support microbial growth and is an independent risk factor for the development of catheter-related bloodstream infections. The risk of infection is increased in patients with malnutrition-associated immunosuppression, long-term use and poor maintenance of intravenous catheters, or immunosuppressive effects of other concomitant conditions or drugs.
- Fat Overload Syndrome: This is a rare condition that has been reported with intravenous lipid emulsions. A reduced or limited ability to metabolize lipids accompanied by prolonged plasma clearance may result in a syndrome characterized by a sudden deterioration in the patient's condition including fever, anemia, leukopenia, thrombocytopenia, coagulation disorders, hyperlipidemia, fatty liver infiltration (hepatomegaly), deteriorating liver function, and central nervous system manifestations (e.g., coma).
- Refeeding Syndrome: Reintroducing calories and protein to severely undernourished patients with PN may result in the refeeding syndrome, characterized by the intracellular shift of potassium, phosphorus, and magnesium as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop.

- Aluminum Toxicity: SMOFLIPID contains no more than 25 mcg/L of aluminum. During prolonged PN administration in patients with renal impairment, the aluminum levels in the patient may reach toxic levels. Preterm infants are at greater risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum. Patients with renal impairment, including preterm infants, who receive parenteral intakes of aluminum at greater than 4 to 5 mcg/kg/day can accumulate aluminum to levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration of PN products.
- Risk of Parenteral Nutrition-Associated Liver Disease (PNALD): PNALD has been reported in patients who receive PN for extended periods of time, especially preterm infants, and can present as cholestasis or steatohepatitis. The exact etiology is unknown and is likely multifactorial. Intravenously administered phytosterols (plant sterols) contained in plant-derived lipid formulations have been associated with development of PNALD, although a causal relationship has not been established. If SMOFLIPID-treated patients develop liver test abnormalities, consider discontinuation or dose reduction.
- Hypertriglyceridemia: Impaired lipid metabolism with hypertriglyceridemia may occur in conditions such as inherited lipid disorders, obesity, diabetes mellitus, and metabolic syndrome.
- Monitoring/Laboratory Tests: Routinely monitor serum triglycerides, fluid and electrolyte status, blood glucose, liver and kidney function, blood count including platelets, and coagulation parameters throughout treatment. Monitoring patients for signs and symptoms of essential fatty acid deficiency (EFAD) is recommended.
- Interference with Laboratory Tests: Content of vitamin K may counteract anticoagulant activity. The lipids contained in this emulsion may interfere with some laboratory blood tests (e.g., hemoglobin, lactate dehydrogenase [LDH], bilirubin, and oxygen saturation) if blood is sampled before lipids have cleared from the bloodstream.

ADVERSE REACTIONS

Most common adverse drug reactions >1% of patients who received SMOFLIPID from clinical trials were nausea, vomiting, hyperglycemia, flatulence, pyrexia, abdominal pain, increased blood triglycerides, hypertension, sepsis, dyspepsia, urinary tract infection, anemia and device-related infection.

Less common adverse reactions in \leq 1% of patients who received SMOFLIPID were dyspnea, leukocytosis, diarrhea, pneumonia, cholestasis, dysgeusia, increased blood alkaline phosphatase, increased gamma-glutamyltransferase, increased C-reactive protein, tachycardia, liver function test abnormalities, headache, pruritis, dizziness, rash and thrombophlebitis.

The following adverse reactions have been identified during post-approval use of SMOFLIPID in countries where it is registered. Infections and Infestations: infection. Respiratory, Thoracic and Mediastinal Disorders: dyspnea.

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.

DRUG INTERACTIONS

Coumarin and Coumarin Derivatives, Including Warfarin: Anticoagulant activity may be counteracted; monitor laboratory parameters.

USE IN SPECIFIC POPULATIONS

- Pregnancy and Lactation: There are no available data on risks associated with SMOFLIPID when used in pregnant or lactating women.
- Pediatric Use: The safety and effectiveness of SMOFLIPID have not been established in pediatric patients.
- Hepatic Impairment: Parenteral nutrition should be used with caution in patients with hepatic impairment. Hepatobiliary disorders are known to develop in some patients without preexisting liver disease who receive PN, including cholestasis, hepatic steatosis, fibrosis, and cirrhosis (PN associated liver disease), possibly leading to hepatic failure.

OVERDOSE

In the event of an overdose, fat overload syndrome may occur. Stop the SMOFLIPID infusion until triglyceride levels have normalized. The effects are usually reversible by stopping the lipid infusion. If medically appropriate, further intervention may be indicated. Lipids are not dialyzable from serum.