ASPEN Lipid Injectable Emulsion Safety Recommendations

Neonate and Pediatric Considerations

Introduction

- Lipid injectable emulsions (ILEs) are intended as a daily source of energy and fatty acids (FAs) in parenteral nutrition (PN) therapy when oral or enteral nutrition is not possible, insufficient, or contraindicated. Considerations for choice of specific ILE products may include intestinal failure, other GI related conditions, bronchopulmonary dysplasia, and retinopathy of prematurity.
- In neonates and pediatric patients, ILE is most often infused via a dedicated intravenous (IV) line that is then Y-site co-infused with the 2-in-1 PN. Some safety concerns for pediatric/neonatal PN include proper filter use for ILE and PN, medication compatibility due to limited IV access, and repackaging of ILE due to small volumes infused.

Indications

There are currently three U.S. FDA approved ILE products for pediatric/neonatal patients. Two additional ILE products are available in the U.S. but do not have a specific FDA approved indication for pediatric patients.

Lipid Injectable Emulsion Products, Characteristics, Abbreviations, and Approval for Use in the U.S.

Intravenous Lipid Emulsion Products	Characteristic (Abbreviation)	FDA Approved Neonatal and Pediatric Indication
Intralipid® (Baxter Healthcare Corporation, Deerfield, Illinois)	Soybean oil-based ILE (SO-ILE)	A source of calories and EFA for patients requiring PN for extended periods of time (usually for more than 5 days) and as a source of EFA for prevention of EFAD syndrome[1]
Nutrilipid® (B. Braun Medical, Inc, Bethlehem, PA)	Soybean oil-based ILE (SO-ILE)	A source of calories and EFA for PN and as a source of FA when a deficiency occurs when oral or enteral nutrition is not possible, insufficient, or contraindicated[2]
Omegaven® (Fresenius-Kabi, Uppsala, Sweden)	Fish oil-based ILE (FO-ILE)	A source of calories and FA in pediatric patients with PN-associated cholestasis[3*]
SMOFlipid® (Fresenius-Kabi, Uppsala, Sweden)	Soybean, MCT, Olive, Fish oil-based ILE (SO,MCT,OO,FO-ILE [multi-oil])	FDA approval not yet attained[4†]
Clinolipid® (Baxter Healthcare Corporation, Deerfield, Illinois)	Olive, Soybean oil-based ILE (OO,SO-ILE, [multi-oil])	FDA approval not yet attained[5†]

Abbreviations: EFA = essential fatty acids, EFAD = essential fatty acid deficiency, FA = fatty acids, MCT = medium chain triglycerides, PN = parenteral nutrition.

* Despite the low content of EFA in FO-ILE, EFAD has not been documented to be associated with use.

† Although not FDA approved, off label use has been studied in these populations.

Prescribing

Published Pediatric Dosage for ILE Products (g/kg per day)

	OO,SO-ILE[6,7]	SO-ILE[1,2]	FO-ILE[3]	SO,MCT,OO,FO-ILE[8]
Preterm Neonate	3†	3	1*	3†
Term Neonate Infant (0-12 months)	3†	2.5-3	1*	3†
Pediatric (1-10 yr)	3†	2.5	1*	2.5-3†
Adolescent (11-17 yr)	2.5†	2-2.5	1*	2-2.5†

Abbreviations: OO,SO-ILE = olive oil, soybean oil ILE, Clinolipid® (Baxter Healthcare Corporation, Deerfield, IL); SO-ILE = soybean oil ILE, Intralipid® (Baxter Healthcare Corporation, Deerfield, IL), Nutrilipid® (B. Braun Medical Inc, Bethlehem, PA); FO-ILE = fish oil ILE = Omegaven® (Fresenius Kabi, Uppsala, Sweden); SO,MCT,OO,FO-ILE = soybean oil, medium chain triglycerides, olive oil, fish oil ILE - SMOFLipid® (Fresenius Kabi, Uppsala, Sweden)

* 1.5 g/kg/day has been used off-label for FO[7]

† Doses for OO,SO-ILE and SO, MCT,OO,FO-ILE are considered off-label, as not FDA approved for pediatrics.

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Summary of Recommendations for ILE use in Neonates and Pediatrics

	Content Summary
Introduction	• ILE is used as an energy source and most often infused separately via Y-site with PN in the neonatal/pediatric population. • Specific safety concerns include in-line filtration, compatibility and stability, medication compatibility, as well as repackaging of commercial product for infusion of small volume.
Indication	• ILE is used for energy and as a source of EFA with a necessity to dose for adequate growth and development. • Choice of specific ILE is dependent on the risk of IFALD, BPD and ROP and other clinical scenarios.
Prescribing	• Dose ILE in g/kg/day. • The infusion rate of ILE should not exceed the maximum rate based on the oil source. • Dose minimization to reduce the risk of IFALD may predispose to EFAD.*
Order Review	• The ILE order must be reviewed for dose (based on indication for use), allergy status, compatibility and stability and ensuring ALL the elements of review are addressed.
Preparation	• There is a risk of contamination when repackaging ILE unless proper procedures are followed. • It is often not possible to compound a total nutrient admixture (TNA) for most pediatric patients due to the increased requirements for calcium and phosphorus and compatibility and stability concerns. Traditional TNA compatibility is derived from SO-ILE. Consult manufacturers for compatibility and stability information for other ILE products.
Administration	• For infusions over 24 hours, divide the daily dose into 2 containers that are changed every 12 hours. • ILE is filtered using a 1.2-micron filter whether co-administered or infused as a TNA. • Photoprotection reduces free radical and lipid peroxides and is recommended when ILE is used in neonates. • There is a risk of inadvertent rapid infusion of ILE when administered separately from PN, which may lead to hypertriglyceridemia and/or fat overload syndrome, especially when the maximum recommended rate is exceeded (>0.15 g/kg/h for SO-ILE). Contact manufacturers for the maximum rate for other ILE. Implement safeguards such as double checks, checklists, and completely setting up the ILE infusion prior to other intravenous fluids including programming to avoid infusion rate errors with PN and other fluids. • Co-administration of medications with ILE is challenging. Compatibility of medications for SO-ILE should not be applied to other oils in ILE unless there is evidence of support. Consult the ILE manufacturer for ILE compatibility with medications.
Transfer of Care	• Whenever possible, use of a TNA product can minimize issues for the caregiver by minimizing preparation time and number of infusion devices. • The specific ILE used can affect compatibility and stability. Prescribers may need to note 'do not interchange' for safe compounding and administration.
Monitoring	• Hypertriglyceridemia is defined as a TG level > 200 mg/dL for patients receiving PN. Avoid exceeding maximum doses and infusion rates of ILE. • Monitor EFA profiles in the malnourished, when there are signs and symptoms of EFAD in those receiving a SO-ILE dose < 1 g/kg/d or when using lipid minimization dosing for any ILE. • Liver function test, including bilirubin, should be monitored for those at risk of IFALD.

Abbreviations: BPD = bronchopulmonary dysplasia, EFA = essential fatty acids, EFAD = essential fatty acid deficiency, IFALD = intestinal failure-associated liver disease, ILE = lipid injectable emulsion, PN = parenteral nutrition, ROP = retinopathy of prematurity, SO-ILE = soybean oil-based ILE, TG = triglyceride, TNA = total nutrient admixtures

**** Dose minimization is product dependent and based on EFA content. Note: For minimum dosing recommendations, contact the individual manufacturers.***

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References

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