March 3, 2014

Dear Valued Baxter Customer,

Baxter Healthcare Corporation is pleased to inform you that effective February 25, 2014, we have removed the allocation on all INTRALIPID 20% (A 20% Intravenous Fat Emulsion) and INTRALIPID 30% (A 30% Intravenous Fat Emulsion) Injections!

In an effort to ensure continuous product supply for our customers and restore the U.S. Lipid Market, Baxter has removed the allocation for all codes as we continue to partner with Fresenius Kabi.

At this time, please continue to place orders for INTRALIPID Injections directly with Baxter. We will continue to evaluate the appropriate timing of distribution through wholesaler and distributor channels. To place an order, please call Baxter’s Center For Service at 1-888-229-0001 or, for online ordering through Baxter’s E-Commerce site, log onto: www.ecomm.baxter.com/csse1.

We’re excited to be able to support you in providing nutrition formulations for your patients.

Please see the below details regarding Indications and Important Risk Information for INTRALIPID Injections.

**Indications**

INTRALIPID 20% (A 20% Intravenous Fat Emulsion) is indicated as a source of calories and essential fatty acids for patients requiring parenteral nutrition for extended periods of time (usually for more than 5 days) and as a source of essential fatty acids for prevention of Essential Fatty Acid Deficiency (EFAD).

INTRALIPID 30% (A 30% Intravenous Fat Emulsion) Pharmacy Bulk Package is indicated for use in a pharmacy admixture program for the preparation of three-in-one or total nutrient admixtures to provide a source of calories and essential fatty acids for patients requiring parenteral nutrition for extended periods of time (usually for more than 5 days) and as a source of essential fatty acids for prevention of Essential Fatty Acid Deficiency (EFAD).

**Important Risk Information**

Deaths in preterm infants after infusion of intravenous fat emulsion have been reported in the medical literature. Autopsy findings included intravascular fat accumulation in the lungs. Treatment of premature and low birth weight infants with intravenous fat emulsion must be based upon careful benefit-risk assessment. Strict adherence to the recommended total daily dose is mandatory; hourly infusion rate should be as slow as possible in each case and should not in any case exceed 1 g fat/kg in 4 hours. Premature and small for gestational age infants have poor clearance of intravenous fat emulsion and increased free fatty acid plasma levels following fat emulsion infusion; therefore, serious consideration must be given to administration of less than the maximum recommended doses in these patients in order to decrease the likelihood of intravenous fat overload. The infant’s ability to eliminate the infused fat from the circulation must be carefully monitored (such as serum triglycerides and/or plasma free fatty acid levels). The lipemia must clear between daily infusions.
• INTRALIPID 30% (A 30% Intravenous Fat Emulsion) Pharmacy Bulk Package is not intended for direct intravenous administration. Diluting INTRALIPID 30% to a 10% or 20% concentration with an IV fluid diluent does not produce a dilution that is equivalent in composition to INTRALIPID 10% or 20% IV fat emulsions and should not be given by direct IV administration.

• The administration of INTRALIPID 20% (A 20% Intravenous Fat Emulsion) and INTRALIPID 30% is contraindicated in patients with disturbances of normal fat metabolism such as pathologic hyperlipemia, lipoid nephrosis or acute pancreatitis if accompanied by hyperlipidemia.

• Exercise caution when administering INTRALIPID 20% and INTRALIPID 30% to patients with severe liver damage, pulmonary disease, anemia or blood coagulation disorders, or when there is danger of fat embolism.

• INTRALIPID 20% and INTRALIPID 30% contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions which contain aluminum.

• Monitor serum triglycerides to determine the patient’s capacity to eliminate the infused fat from the circulation. Overdosage must be avoided. During long-term intravenous nutrition with INTRALIPID 20% or INTRALIPID 30%, liver function tests should be performed and therapy withdrawn if the liver becomes impaired.

• Frequent (some advise daily) platelet counts should be done in neonatal patients receiving parenteral nutrition with INTRALIPID 20% or INTRALIPID 30%.

• Frequent adverse events include sepsis due to contamination of the IV catheter and vein irritation may result in thrombophlebitis by concurrently infused hypertonic solutions. Less frequent adverse reactions reported <1% in clinical trials are:
  o Immediate or early: dyspnea, cyanosis, allergic reactions, hyperlipemia, hypercoagulability, nausea, vomiting, headache, flushing, increase in temperature, sweating, sleepiness, pain in the chest and back, slight pressure over the eyes, dizziness, and irritation at the site of infusion and rarely thrombocytopenia in neonates.
  o Delayed: hepatomegaly, jaundice due to central lobular cholestasis, splenomegaly, thrombocytopenia, leukopenia, transient increases in liver function tests, and overloading syndrome (focal seizures, fever, leukocytosis, hepatomegaly, splenomegaly and shock).
  o The deposition of a brown pigmentation in the reticuloendothelial system called “intravenous fat pigment” has been reported. The causes and significance are unknown.

Please see attached package insert for full Prescribing Information including Boxed Warning.

Sincerely,

Thomas J. Progar
Marketing Strategy and Operations
Medication Delivery, U.S. Region
Baxter Healthcare Corporation

Baxter is a registered trademark of Baxter International Inc.
Intralipid is a registered trademark of Fresenius Kabi AB.

USMP/175/14-0001 3/14
Intralipid® 20% is a sterile, non-pyrogenic fat emulsion prepared for intravenous administration as a source of calories and essential fatty acids. It is made up of 20% Soybean Oil, 1.2% Egg Yolk Phospholipids, 2.25% Glycerin, and Water for Injection. In addition, sodium hydroxide has been added to adjust the pH so that the final product pH is 8. pH range is 6 to 8.9. The soybean oil is a refined natural product consisting of a mixture of neutral triglycerides of predominantly unsaturated fatty acids with the following structure:

\[
\begin{align*}
\text{Linoleic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2 \\
\text{Oleic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2 \\
\text{Palmitic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2 \\
\text{Linolenic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2 \\
\text{Stearic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2
\end{align*}
\]

where R-C, R-C, and R-C are saturated and unsaturated fatty acid residues. The major component fatty acids are linoleic (44-62%), oleic (19-30%), palmitic (7-14%), linolenic (4-11%) and stearic (1.4-5.5%). These fatty acids have the following chemical and structural formulas:

\[
\begin{align*}
\text{Linoleic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2 \\
\text{Oleic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2 \\
\text{Palmitic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2 \\
\text{Linolenic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2 \\
\text{Stearic acid} & : \text{C}_\text{H}_\text{S}_\text{O}_2
\end{align*}
\]

Clinical Pharmacology
Intralipid® 20% is metabolized and utilized as a source of energy causing an increase in heat production, decrease in respiratory quotient and increase in oxygen consumption. The infused fat particles are cleared from the blood stream in a manner thought to be comparable to the clearing of chylomicrons. Intralipid® 20% will prevent the biochemical lesions of essential fatty acid deficiency (EFAD), and correct the clinical manifestations of the EFAD syndrome.

Indications and Use
Intralipid® 20% is a source of calories and essential fatty acids for patients requiring parenteral nutrition for extended periods of time (usually for more than 5 days) and as a source of essential fatty acids for prevention of EFAD.

Contraindications
The administration of Intralipid® 20% is contraindicated in patients with disturbances of normal fat metabolism such as pathologic hyperlipemia, lipid nephrosis or acute pancreatitis if accompanied by hyperlipidemia.

Warnings
Deaths in preterm infants after infusion of Intravenous fat emulsion have been reported in the medical literature. Autopsy findings included intravascular fat accumulation in the lungs. Treatment of premature and low birth weight infants with Intravenous fat emulsion must be based upon careful benefit-risk assessment. Strict adherence to the recommended total daily dose is mandatory; hourly infusion rate should be as slow as possible in each case and should not in any case exceed 1 g fat/kg in four hours. Premature and small for gestational age infants have poor clearance of Intravenous fat emulsion and increased free fatty acid plasma levels following fat emulsion infusion; therefore, serious consideration must be given to administration of less than the maximum recommended doses in these patients in order to decrease the likelihood of Intravenous fat overload. The infant's ability to eliminate the infused fat from the circulation must be carefully monitored (such as serum triglycerides and/or plasma free fatty acid levels). The lipemia must clear between daily infusions.
Caution should be exercised in administering Intralipid® 20% (A 20% Intravenous Fat Emulsion) to patients with severe liver damage, pulmonary disease, anemia or blood coagulation disorders, or when there is danger of fat embolism.

**WARNING:** This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum. Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

**PRECAUTIONS**

When Intralipid® 20% is administered, the patients capacity to eliminate the infused fat from the circulation must be monitored by use of an appropriate laboratory determination of serum triglycerides. Overdosage must be avoided. During long term intravenous nutrition with Intralipid® 20%, liver function tests should be performed. If these tests indicate that liver function is impaired, the therapy should be withdrawn.

Frequent (some advise daily) platelet counts should be done in neonatal patients receiving parenteral nutrition with Intralipid® 20%.

Drug product contains no more than 25 mcg/L of aluminum.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Studies with Intralipid® have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility.

**Pregnancy Category C:** Animal reproduction studies have not been conducted with Intralipid®. It is also not known whether Intralipid® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Intralipid® should be given to a pregnant woman only if clearly needed.

**Nursing Mothers:** Caution should be exercised when Intralipid® is administered to a nursing woman.

**Pediatric Use:** See DOSAGE AND ADMINISTRATION.

**AVOID OVERDOSE ABSOLUTELY.**

**ADVERSE REACTIONS**

The adverse reactions observed can be separated into two categories:

1. Those more frequently encountered are due: either to contamination of the intravenous catheter and result in sepsis, or to vein irritation by concurrently infused hypertonic solutions and may result in thrombophlebitis. These adverse reactions are inseparable from the hyperalimentation procedure with or without Intralipid® 20% (A 20% I.V. Fat Emulsion).

2. Less frequent reactions more directly related to Intralipid® 20% are: a) immediate or early adverse reactions, each of which has been reported to occur in clinical trials, in an incidence of less than 1%: dyspnea, cyanosis, allergic reactions, hyperlipemia, hypercoagulability, nausea, vomiting, headache, flushing, increase in temperature, sweating, sleepiness, pain in the chest and back, slight pressure over the eyes, dizziness, and irritation at the site of infusion, and, rarely, thrombocytopenia in neonates; b) delayed adverse reactions such as hepatitis, jaundice due to central lobular cholestasis, splenomegaly, thrombocytopenia, leukopenia, transient increases in liver function tests, and overloading syndrome (focal seizures, fever, leukocytosis, hepatomegaly, splenomegaly and shock).

The deposition of a brown pigmentation in the reticuloendothelial system, the so-called "intravenous fat pigment," has been reported in patients infused with Intralipid® 20%. The causes and significance of this phenomenon are unknown.

**OVERDOSE**

In the event of fat overload during therapy, stop the infusion of Intralipid® 20% until visual inspection of the plasma, determination of triglyceride concentrations, or measurement of plasma light-scattering activity by nephelometry indicates the lipid has cleared. Re-evaluate the patient and institute appropriate corrective measures. See WARNINGS and PRECAUTIONS.

**DOSAGE AND ADMINISTRATION**

Intralipid® 20% should be administered as a part of intravenous nutrition via peripheral vein or by central venous infusion.

**Adult Patients**

The initial rate of infusion in adults should be 0.5 ml/minute for the first 15 to 30 minutes of infusion. If no untoward reactions occur (see ADVERSE REACTIONS section), the infusion rate can be increased to 1 ml/minute. Not more than 500 ml of Intralipid® 20% should be infused into adults on the first day of therapy. If the patient has no untoward reactions, the dose can be increased on the following day. The daily dosage should not exceed 2.5 g of fat/kg of body weight (12.5 ml of Intralipid® 20% per kg). Intralipid® 20% (A 20% I.V. Fat Emulsion) should make up no more than 60% of the total caloric input to the patient. Carbohydrate and a source of amino acids should comprise the remaining caloric input.

**Pediatric Patients**

The dosage for premature infants starts at 0.5 g fat/kg body weight/24 hours (2.5 ml Intralipid® 20%) and may be increased in relation to the infant's ability to eliminate fat. The maximum dosage recommended by the American Academy of Pediatrics is 5 g fat/kg/24 hours.

The initial rate of infusion in older pediatric patients should be no more than 0.05 ml/minute for the first 10 to 15 minutes. If no untoward reactions occur, the rate can be changed to permit infusion of 0.5 ml of Intralipid® 20%/kg/hour. The daily dosage should not exceed 3 g of fat/kg of body weight. Intralipid® 20% should make up no more than 60% of the total caloric input to the patient. Carbohydrate and a source of amino acids should comprise the remaining caloric input.

**Essential Fatty Acid Deficiency**

When Intralipid® 20% is administered to correct essential fatty acid deficiency, eight to ten percent of the caloric input should be supplied by Intralipid® 20% in order to provide adequate amounts of linoleic and linolenic acids. When EFAD occurs together with stress, the amount of Intralipid® 20% needed to correct the deficiency may be increased.

**Administration**

See MIXING GUIDELINES AND LIMITATIONS section for information regarding mixing this fat emulsion with other parenteral fluids.

Intralipid® 20% can be infused into the same central or peripheral vein as carbohydrate/amino acids solutions by means of a Y-connector near the infusion site. This allows for mixing of the emulsion immediately before entering the vein or for alternation of each parenteral fluid. If infusion pumps are used,
flow rates of each parenteral fluid should be controlled with a separate pump. Fat emulsion may also be infused through a separate peripheral site. Filters of less than 1.2 micron pore size must not be used with Intralipid® 20%.

Conventional administration sets and TPN pooling bags contain polyvinyl chloride (PVC) components that have DEHP (diethylhexyl phthalate) as a plasticizer. Fat-containing fluids such as Intralipid® 20% extract DEHP from these PVC components and it may be advisable to consider infusion of Intralipid® 20% through a non-DEHP administration set.

Do not use any bag in which there appears to be an oiling on the surface of the emulsion.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Whenever solution and container permit:

**MIXING GUIDELINES AND LIMITATIONS**

Investigations have been conducted which demonstrate the compatibility of Intralipid® 20% (A 20% I.V. Fat Emulsion) when properly mixed with either Novamine® or 8.5% Travasol® or 10% Travasol® Amino Acid Injections without Electrolytes for use in TPN therapy.

The following proper mixing sequence must be followed to minimize pH related problems by ensuring that typically acidic Dextrose Injections are not mixed with lipid emulsions alone:

1. Transfer Dextrose Injection to the TPN Admixture Container
2. Transfer Amino Acid Injection
3. Transfer Intralipid® 20% (A 20% Intravenous Fat Emulsion)

Note: Amino Acid Injection, Dextrose Injection and Intralipid® 20% may be simultaneously transferred to the admixture container. Admixing should be accompanied by gentle agitation to avoid localized concentration effects.

These admixtures should be used promptly with storage under refrigeration (2-8°C) not to exceed 24 hours and must be completely used within 24 hours after removal from refrigeration. It is essential that the admixture be prepared using strict aseptic techniques as this nutrient mixture is a good growth medium for microorganisms.

Additives other than those named above may be incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist, if available. If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Do not store solutions containing additives (e.g., vitamins and minerals).

Additives must not be added directly to Intralipid® 20% and in no case should Intralipid® 20% be added to the TPN container first. Bags should be shaken gently after each addition to minimize localized concentration.

Supplemental electrolytes, trace metals or multivitamins may be required in accordance with the prescription of the attending physician.

The prime destabilizers of emulsions are excessive acidity (low pH) and inappropriate electrolyte content. Careful consideration should be given to additions of divalent cations (Ca++ and Mg++) which have been shown to cause emulsion instability. Amino acid solutions exert a buffering effect protecting the emulsion. The admixture should be inspected carefully for “breaking or oozing out” of the emulsion. “Breaking or oozing out” is described as the separation of the emulsion and can be visibly identified by a yellowish streaking or the accumulation of yellow droplets in the admixed emulsion. The admixture should also be examined for particulates. The admixture must be discarded if any of the above is observed.

**HOW SUPPLIED**

Intralipid® 20% is supplied as a sterile emulsion in the following fill sizes: 100 mL, 250 mL, 500 mL and 1000 mL.

- 100 mL: 0338-0519-48
- 250 mL: 0338-0519-02
- 500 mL: 0338-0519-03
- 1000 mL: 0338-0519-04

**STORAGE**

Intralipid® 20% should not be stored above 25°C (77°F). Do not freeze Intralipid® 20%. If accidentally frozen, discard the bag.

**REFERENCES**


(Rev April 2007)

Manufactured for
Baxter Healthcare Corporation
Clintec Nutrition Division
Deerfield, IL 60015 USA

Manufactured by
Fresenius Kabi,
Uppsala, Sweden

Intralipid® is a registered trademark of Fresenius Kabi AB.
Novamine® is a registered trademark of Fresenius Kabi AB.
Travasol® is a registered trademark of Baxter Healthcare Corporation.
1. The integrity indicator (Oxalert™) A should be inspected before removing the overpouch. If the indicator is black the overpouch is damaged and the product should be discarded.

2. Remove the overwrap by tearing at the notch and pulling down along the container. The Oxalert™ sachet A and the oxygen absorber B should be disposed.

3. Remove set port cover lifting ring with thumb and forefinger and pulling upwards.

4. Use a non-vented infusion set or close the air vent on a vented set. Follow the instructions for use for the infusion set. Use a spike conforming to ISO 8536-4, diameter 5.6 ± 0.1 mm.

5. The bag should be port side up when the infusion set is attached. Insert the spike straight into the set port. Twist and push the spike through the diaphragm. Do not spike bag while the bag is hanging on the IV pole.

6. The step of the spike (shown by the arrow) should not be inserted into the port.
7. To hang the bag, invert and place hanger through container notch.
Intralipid® 30%
A 30% I.V. Fat Emulsion
In Excel® Container

Pharmacy Bulk Package
Not For Direct Infusion

DESCRIPTION
Intralipid® 30% (A 30% I.V. Fat Emulsion) Pharmacy Bulk Package is a sterile, non-pyrogenic fat emulsion intended as a source of calories and essential fatty acids for use in a pharmacy admixture program. It is made up of 30% Soybean Oil, 12% Egg Yolk Phospholipids, 17% Glycerin, and Water for Injection. In addition, sodium hydroxide has been added to adjust the pH so that the final product pH is 8. pH range is 6 to 9.9.

Intralipid® 30% Pharmacy Bulk Package is not intended for direct infusion. It is a sterile dosage form which contains several single doses for use in the preparation of three-in-one or total nutrient admixtures (TNAs) in a pharmacy admixture program.

The soybean oil is a refined natural product consisting of a mixture of neutral triglycerides of predominantly unsaturated fatty acids with the following structure:

\[ \begin{align*}
\text{CH}_2\text{OOCR}_1 & \\
\text{RCOOCH}_2 & \\
\text{CH}_3\text{OOCR}_3 & \\
\end{align*} \]

where \( R_1, R_2, \) and \( R_3 \) contain saturated and unsaturated fatty acid residues.

The major component fatty acids are linoleic (44-62%), oleic (19-30%), palmitic (7-14%), linolenic (4-11%), and stearic (1.4-5.5%). These fatty acids have the following chemical and structural formulas:

**Linoleic acid**
\[ \begin{align*}
\text{CH}_2\text{OOCR}_1 & \\
\text{RCOOCH}_2 & \\
\text{CH}_3\text{OOCR}_3 & \\
\end{align*} \]

**Oleic acid**
\[ \begin{align*}
\text{CH}_2\text{OOCR}_1 & \\
\text{RCOOCH}_2 & \\
\text{CH}_3\text{OOCR}_3 & \\
\end{align*} \]

**Palmitic acid**
\[ \begin{align*}
\text{CH}_2\text{OOCR}_1 & \\
\text{RCOOCH}_2 & \\
\text{CH}_3\text{OOCR}_3 & \\
\end{align*} \]

**Linolenic acid**
\[ \begin{align*}
\text{CH}_2\text{OOCR}_1 & \\
\text{RCOOCH}_2 & \\
\text{CH}_3\text{OOCR}_3 & \\
\end{align*} \]

Purified egg phosphatides are a mixture of naturally occurring phospholipids which are isolated from the egg yolk. These phospholipids have the following general structure:

\[ \begin{align*}
\text{CH}_2\text{OOCR}_1 & \\
\text{RCOOCH}_2 & \\
\text{CH}_3\text{OOCR}_3 & \\
\end{align*} \]

\[ \begin{align*}
\text{CH}_2\text{OOCR}_1 & \\
\text{RCOOCH}_2 & \\
\text{CH}_3\text{OOCR}_3 & \\
\end{align*} \]

\[ \begin{align*}
\text{CH}_2\text{OOCR}_1 & \\
\text{RCOOCH}_2 & \\
\text{CH}_3\text{OOCR}_3 & \\
\end{align*} \]

**Phosphatidylcholine**

**Phosphatidylethanolamine**

Glycerin is chemically designated \( \text{C}_3\text{H}_5\text{O}_3 \) and is a clear colorless, hygroscopic syrupy liquid. It has the following structural formula:

\[ \begin{align*}
\text{CH}_2\text{OH} & \\
\text{HOCH}_2 & \\
\text{CH}_2\text{OH} & \\
\end{align*} \]

Intralipid® 30% (A 30% I.V. Fat Emulsion) has an osmolality of approximately 310 mOsmol/kg water which represents 200 mOsmol/1 liter of emulsion) and contains emulsified fat particles of approximately 0.5 micron size. The total caloric value, including fat, phospholipid and glycerin, is 3.0 kcal per mL of Intralipid® 30%. The phospholipids present contribute 44 milligrams or approximately 1.5 mmol of phosphorus per 100 mL of the emulsion.

The primary container is manufactured from Excel® film, a polypropylene based material comprised of three co-extruded layers. The plastic container is made from multilayered film specifically designed for parenteral drugs. It contains no plasticizers and exhibits virtually no leachables. The solution contact layer is a rubberized copolymer of ethylene and propylene. The container is nontoxic and biologically inert. The container-solution unit is a closed system and is not dependent upon entry of external air during administration. The container is overwrapped to provide protection from the physical environment and to provide an additional moisture barrier when necessary.

CLINICAL PHARMACOLOGY

Intralipid® is metabolized and utilized as a source of energy causing an increase in heat production, decrease in respiratory quotient and increase in oxygen consumption. The infused fat
particles are cleared from the blood stream in a manner thought to be comparable to the clearing of chylomicrons. Intralipid® will prevent the biochemical lesions of essential fatty acid deficiency (EFAD), and correct the clinical manifestations of the EFAD syndrome.

INDICATIONS AND USAGE
Intralipid® 30% Pharmacy Bulk Package is indicated for use in a pharmacy admixture program for the preparation of three-in-one or total nutrient admixtures (TNAs) to provide a source of calories and essential fatty acids for patients requiring parenteral nutrition for extended periods of time (usually for more than 5 days) and as a source of essential fatty acids for prevention of EFAD.

CONTRAINDICATIONS
INTRALIPID® 30% PHARMACY BULK PACKAGE IS NOT INTENDED FOR DIRECT INTRAVENOUS ADMINISTRATION. DILUTING INTRALIPID® 30% TO A 10% OR 20% CONCENTRATION WITH AN INTRAVENOUS FLUID SUCH AS NORMAL SALINE OR OTHER DILUENT DOES NOT PRODUCE A DILUTION THAT IS EQUIVALENT IN COMPOSITION TO INTRALIPID® 10% OR 20% I.V. FAT EMULSIONS, AND SUCH A DILUTION SHOULD NOT BE GIVEN BY DIRECT INTRAVENOUS ADMINISTRATION (FOR EXAMPLE, THROUGH A Y-CONNECTOR).

The administration of Intralipid® is contraindicated in patients with disturbances of normal fat metabolism such as pathologic hyperlipemia, lipid nephrosis or acute pancreatitis if accompanied by hyperlipidemia. Intralipid® 30% (A 30% I.V. Fat Emulsion) is not intended for direct intravenous infusion.

WARNINGS

Deaths in preterm infants after infusion of intravenous fat emulsion have been reported in the medical literature. Autopsy findings included intravascular fat accumulation in the lungs. Treatment of premature and low birth weight infants with Intravenous Fat emulsion must be based upon careful benefit-risk assessment. Strict adherence to the recommended total daily dose is mandatory; hourly infusion rate should be as slow as possible in each case and the total fat should not in any case exceed 1 g fat/kg in four hours. Premature and small for gestational age infants have poor clearance of Intravenous Fat emulsion and increased free fatty acid plasma levels following fat emulsion infusion; therefore, serious consideration must be given to administration of less than the maximum recommended doses in these patients in order to decrease the likelihood of intravenous fat overload. The infant’s ability to eliminate the infused fat from the circulation must be carefully monitored (such as serum triglycerides and/or plasma free fatty acid levels). The lipemia must clear between daily infusions.

Caution should be exercised in administering of Intralipid® 30% to patients with severe liver damage, pulmonary disease, anemia or blood coagulation disorders, or when there is danger of fat embolism.

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS
When Intralipid® is administered, the patients capacity to eliminate the infused fat from the circulation must be monitored by use of an appropriate laboratory determination of serum triglycerides. Overdose must be avoided. During long term intravenous nutrition with Intralipid®, liver function tests should be performed. If these tests indicate that liver function is impaired, the therapy should be withdrawn. Frequent (some advise daily) platelet counts should be done in neonatal patients receiving parenteral nutrition with Intralipid®.

Drug product contains no more than 25 mcg/L of aluminum.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Studies with Intralipid® have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility.

Pregnancy Category C: Animal reproduction studies have not been conducted with Intralipid®. It is also not known whether Intralipid® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Intralipid® should be given to a pregnant woman only if clearly needed.

Nursing Mothers: Caution should be exercised when Intralipid® is administered to a nursing woman.

Pediatric Use: See DOSAGE AND ADMINISTRATION.

AVOID OVERDOSE ABSOLUTELY.

ADVERSE REACTIONS

The adverse reactions observed can be separated into two classes:

1. Those more frequently encountered are due either to a) contamination of the intravenous catheter and result in sepsis, or to b) vein irritation by concurrently infused hypertonic solutions and may result in thromboembolitis. These adverse reactions are inseparable from the hyperalimentation procedure with or without Intralipid®.

2. Less frequent reactions more directly related to Intralipid® are:
   a) immediate or early adverse reactions, each of which has been reported to occur in clinical trials, in an incidence of less than 1%: dyspnea, cyanosis, allergic reactions, hyperlipemia, hypercoagulability, nausea, vomiting, headache, flush, increase in temperature, sweating, sleepiness, pain in the
CHEST AND BACK, SLIGHT PRESSURE OVER THE EYES, DIZZINESS, AND
IRRITATION AT THE SITE OF INFUSION, AND, RARELY, THROMBOCYTOPENIA
IN NEONATES; B) DELAYED ADVERSE REACTIONS SUCH AS HEPATOMEGALY,
JAUNDICE DUE TO CENTRAL LOBULAR CHOLESTASIS, SPLENOMEGALY,
THROMBOCYTOPENIA, LEUKOPENIA, TRANSIENT INCREASES IN LIVER
FUNCTION TESTS, AND OVERLOADING SYNDROME (FOCAL SEIZURES,
FEVER, LEUKOCYTOSIS, HEPATOMEGALY, SPLENOMEGALY AND
SHOCK).

The deposition of a brown pigmentation in the reticuloendothelial system, the so-called "intravenous fat pigment," has been reported in patients infused with intralipid®. The causes and significance of this phenomenon are unknown.

OVERDOSE

In the event of fat overload during therapy, stop the infusion containing intralipid® 30% (A 30% I.V. Fat Emulsion) until visual inspection of the plasma, determination of triglyceride concentrations, or measurement of plasma light-scattering activity by nephelometry indicates the lipid has cleared. Re-evaluate the patient and institute appropriate corrective measures. See WARNINGS and PRECAUTIONS.

DOSEAGE AND ADMINISTRATION

Intralipid® 30% (A 30% I.V. Fat Emulsion) Pharmacy Bulk Package should be administered only as a part of a three-in-one or total nutrient admixture via peripheral vein or by central venous infusion.

DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE

INTRALIPID® 30% (A 30% I.V. Fat Emulsion) PHARMACY BULK
PACKAGE IS NOT INTENDED FOR DIRECT INFUSION. The container
closure may be penetrated only once using a suitable sterile
transfer device or dispensing set which allows measured dispens-
ing of the contents. The Pharmacy Bulk Package is to be used
only in a suitable work area such as a laminar flow hood (or an
equivalent clean air compounding area). Once the closure is
penetrated, the contents should be dispensed as soon as possible;
the transfer of contents to suitable TPN admixture containers
must be completed within 4 hours of closure penetration. The
tube should be stored below 25°C (77°F) after the closure has
been entered. Date and time of container entry should be noted
in the area designated on the container label.

Admixtures made using intralipid 30% should be used promptly.
See MIXING GUIDELINES AND LIMITATIONS section for admixture
storage recommendations.

ADULT PATIENTS

The initial infusion rate of the nutrient admixture in adults
should be the equivalent of 0.1 g fat/minute for the first 15
to 30 minutes of infusion. If no untoward reactions occur (see
ADVERSE REACTIONS section), the infusion rate of the nutrient
admixture can be increased to be equivalent to 0.2 g fat/minute.
For adults, the admixture should not contain more than
330 mL of Intralipid® 30% on the first day of therapy. If the
patient has no untoward reactions, the dose can be increased
on the following day. The daily dosage should not exceed 2.5 g of
fat/kg of body weight (83 mL of Intralipid® 30% per kg). Intralipid® should make up no more than 60% of the total caloric input to the patient. Carbohydrate and a source of amino acids should comprise the remaining caloric input.

PEDIATRIC PATIENTS

The dosage for premature infants starts at 0.5 g fat/kg body
weight/24 hours (1.7 mL) Intralipid® 30% and may be increased
in relation to the infant's ability to eliminate fat. The maximum
dosage recommended by the American Academy of Pediatrics
is 3 g fat/kg/24 hours.1

The initial rate of infusion of the nutrient admixture in older
pediatric patients should be no more than 0.01 g fat/minute
for the first 10 to 15 minutes. If no untoward reactions occur,
the rate can be changed to permit infusion of 0.1 g of fat/kg/
hour. The daily dosage should not exceed 3 g of fat/kg of body
weight. Intralipid® should make up no more than 60% of the
total caloric input to the patient. Carbohydrate and a source of
amino acids should comprise the remaining caloric input.

ESSENTIAL FATTY ACID DEFICIENCY

When Intralipid® is administered to correct essential fatty acid
deficiency, eight to ten percent of the caloric input should be
supplied by Intralipid® in order to provide adequate amounts of
linoleic and linolenic acids. When EFAD occurs together with
stress, the amount of Intralipid® needed to correct the
deficiency may be increased.

ADMINISTRATION

See MIXING GUIDELINES AND LIMITATIONS section for informa-
tion regarding mixing this fat emulsion with other parenteral
fluids. INTRALIPID® 30% (A 30% I.V. Fat Emulsion) is not for direct
infusion. It must be infused as part of an admixture into a central
or peripheral vein.

The flow rate of the admixture should be controlled with an
infusion pump. Filters of less than 1.2 micron pore size must
not be used with admixtures containing Intralipid® 30%.

Conventional administration sets and TPN pooling bags contain
dichloroethylene (PVC) components that have DEHP (diethyl
hexyl phthalate) as a plasticizer. Fat-containing fluids such as
intralipid® extract DEHP from these PVC components. Therefore
it may be advisable to use a non-DEHP administration set for
infusing admixtures which contain Intralipid®.

Do not use any bag in which there appears to be an oiling out
on the surface of the emulsion.

Parenteral drug products should be inspected visually for
particulate matter and discoloration prior to administration.
Whenever solution and container permit.

MIXING GUIDELINES AND LIMITATIONS

INTRALIPID® 30% PHARMACY BULK PACKAGE IS NOT INTENDED
FOR DIRECT INFUSION. It must be combined with total parenteral
nutrition (TPN) fluids so that the resulting admixture has a final
calorie concentration of not more than 20% fat (0.2 g fat per mL of
admixture). The following table may be used as a guide:

<p>| 330 | 737 |</p>
<table>
<thead>
<tr>
<th>Volume of Intralipid® 30%</th>
<th>Required Minimum</th>
<th>Final Volume of Admixture</th>
<th>Final Fat Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mL</td>
<td>+ 0.5 mL</td>
<td>= 1.5 mL</td>
<td>20%</td>
</tr>
<tr>
<td>100 mL</td>
<td>+ 50 mL</td>
<td>= 150 mL</td>
<td>20%</td>
</tr>
<tr>
<td>250 mL</td>
<td>+ 125 mL</td>
<td>= 375 mL</td>
<td>20%</td>
</tr>
<tr>
<td>500 mL</td>
<td>+ 250 mL</td>
<td>= 750 mL</td>
<td>20%</td>
</tr>
</tbody>
</table>

Investigations have been conducted which demonstrate the compatibility of Intralipid® 30% when properly mixed with either Novamine® (8.5%, 11.4% or 15%), or 8.5% Travasol® or 10% Travasol® Amino Acid Injections for use in Total Parenteral Nutrition (TPN) therapy. Because of the potential for life threatening events, caution should be taken to ensure that precipitates have not formed in any parenteral nutrition mixture. Perform all manipulations in a suitable work area, such as a laminar flow hood.

**Failure to follow the Mixing Guidelines and Limitations below, including recommended storage temperature, storage time, order of mixing, etc., may result in an unstable admixture.**

The following proper mixing sequence must be followed to minimize pH related problems by ensuring that typically acidic Dextrose injections are not mixed with lipid emulsions alone:
1. Transfer Dextrose Injection to the TPN admixture Container
2. Transfer Amino Acid Injection
3. Transfer Intralipid® 30% (A 30% I.V. Fat Emulsion)

Note: Amino Acid Injection, Dextrose injection and Intralipid® may be simultaneously transferred to the admixture container. Adminixture should be accompanied by gentle agitation to avoid localized concentration effects. These admixtures should be used promptly with storage under refrigeration (2-8°C) not to exceed 24 hours and must be completely used within 24 hours after removal from refrigeration.

It is essential that the admixture be prepared using strict aseptic techniques as this nutrient mixture is a good growth medium for microorganisms.

Additives other than those named above may be incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist. If in the informed judgement of the prescribing physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Do not store solutions containing additives (e.g., vitamins and minerals).

Additives must not be added directly to Intralipid® and in no case should Intralipid® be added to the TPN container first. Bags should be shaken gently after each addition to minimize localized concentration.

Supplemental electrolytes, trace metals or multivitamins may be required in accordance with the prescription of the attending physician.

The prime destabilizers of emulsions are excessive acidity (low pH) and inappropriate electrolyte content. Careful consideration should be given to additions of divalent cations (Ca++ and Mg++) which have been shown to cause emulsion instability. Amino acid solutions exert a buffering effect protecting the emulsion.

The admixture should be inspected carefully for "breaking or oiling out" of the emulsion. "Breaking or oiling out" is described as the separation of the emulsion and can be visibly identified by a yellowish streaking or the accumulation of yellowish droplets in the admixed emulsion. The admixture should also be examined for particulates. The admixture must be discarded if any of the above is observed.

**HOW SUPPLIED**
Intralipid® 30% (A 30% I.V. Fat Emulsion) is supplied as a sterile emulsion in a Pharmacy Bulk Package in the following fill sizes:

- 500 mL: 0338-0520-03

**STORAGE**
Intralipid® 30% should not be stored above 25°C (77°F). Do not freeze Intralipid® 30%. If accidentally frozen, discard the bag.

**REFERENCES**

(Rev April 2000)

Manufactured for
Baxter Healthcare Corporation
Clinitec Nutrition Division
Deerfield, IL 60015 USA

Manufactured by
Fresenius Kabi,
Upplands Väsby, Sweden

Intralipid® is a registered trademark of Fresenius Kabi AB.
Novamine® is a Registered trademark of Fresenius Kabi AB.
Travasol® is a registered trademark of Baxter Healthcare Corporation.
1. The integrity indicator (Oxalert™) A should be inspected before removing the overpouch. If the indicator is black the overpouch is damaged and the product should be discarded.

2. Remove the overwrap by tearing at the notch and pulling down along the container. The Oxalert™ sachet A and the oxygen absorber B should be disposed.

3. Remove set port cover lifting ring with thumb and forefinger and pulling upwards.