Amendment date: 28 May 2021
Approved date: 23 July 2021

APPROVED PROFESSIONAL INFORMATION FOR HUMAN MEDICINES

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

Lipovenoes 10 % PLR

Emulsion for parenteral infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 ml contains:

Soybean oil 10,0 g

Egg lecithin 0,6 g

Glycerol 2,5 g

Contains sugar (as glycerol 2,5 g)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

White, homogeneous emulsion

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Lipovenoes 10 % PLR is indicated as a source of energy and essential fatty acids as part of total parenteral nutrition regimens either alone or in conjunction with amino acids and carbohydrate solutions.

4.2 Posology and method of administration

Lipovenoes 10 % PLR may be administered along with other amino-acid and/or carbohydrate solutions, but through separate infusion systems and veins. However, should a simultaneous infusion of two solutions via a common end-section (by-pass, Y-tube) be considered clinically, the compatibility of both solutions must be ensured at all costs.

Lipovenoes 10 % PLR is administered intravenously via a peripheral vein in short-term nutrition, and via a central venous line during longer periods of nutrition.

Intravenous solutions or other medicines must not be added directly to the Lipovenoes 10 % PLR bottle as this may destabilise or break the emulsion.

The contents of an opened bottle must be used immediately and cannot be kept for future use.

For neonates, infants and children:

If not otherwise prescribed, 1 to 2 g fat/kg weight/day = 10 to 20 ml Lipovenoes 10 % PLR/kg body weight/day.

With increased energy requirements:

Up to 3 g fat/kg weight/day = 30 ml Lipovenoes 10 % PLR/kg body weight/day.

The dosage and dosage increments are governed by the infant's ability to eliminate fat which should be checked daily.

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed (see sections 4.4, 6.3 and 6.6).

For adults:

If not otherwise prescribed, 1 to 2 g fat/kg weight/day = 10 to 20 ml Lipovenoes 10 % PLR/kg body weight/day.

Infusion rate:

A maximum of 0,125 g fat/kg body weight /hour = 1,25 ml/kg body weight/hour is infused.

However, at the beginning of parenteral nutrition with fat, a slow dosage with a maximum of 0,05 g fat/kg body weight/hour is recommended.

At a body weight of 70 kg, infusion is begun with 10 drops/minute and increased gradually after 30 minutes to a maximum of 26 drops per minute.

Fat elimination test:

In cases where daily infusions of intravenous fat for more than one week are indicated, the ability of the patients to eliminate administered fat should be tested.

Before starting the infusion, a fasting blood sample is taken for ESR (citrate). The sample is centrifuged at 1 200 to 1 500 rpm. If the plasma is milky or markedly opalescent, the planned infusion should be postponed.

See Section 4.4 “Warnings and special precautions”.

4.3 Contraindications

- Liver damage
- Metabolic disturbances such as lipoprotein lipase deficiency
- Impaired lipid metabolism, including lipoid nephrosis and hyperlipidaemia
- Blood dyscrasias
- Severe haemorrhagic diathesis
- Uncontrolled diabetes mellitus
- Pregnancy during the first trimester
- Hypersensitivity to egg-, soya- or peanut protein or to any of the active substances or excipients. (See section 4.4)
- All acute and life-threatening diseases such as collapse and shock, recent cardiac infarction, stroke, embolism and undefined coma status

- General contra-indications for parenteral nutrition include hypokalaemia, hyperhydration and hypotonic dehydration

The application of Lipovenoes 10 % PLR in paediatric patients with hyperbilirubinaemia has to be monitored carefully (benefit - risk ratio). Bilirubin has to be checked closely when administering a fat emulsion.

There is a risk of kernicterus.

4.4 Special warnings and precautions for use

For intravenous use only.

Soya-bean oil emulsion should not be given to patients with severe liver disease, acute shock or hyperlipidaemia, or with other conditions where the ability to absorb or metabolise fat may be impaired. However, if administration is considered necessary in such patients, the fat elimination capacity must be checked daily.

The patient's ability to eliminate administered fat should govern the dosage. (See section 4.2). The serum triglyceride level has to be checked daily. The blood sugar profile, acid-base metabolism, electrolytes and water balance must be checked at regular intervals. The triglyceride concentration in serum under infusion of fat should not exceed 3 mmol/l for adults and 1,7 mmol/l for children.

When intravenous soya oil emulsion is administered over a prolonged period, the patient's elimination capacity of the fat should be investigated to ensure that hyperlipidaemia does not occur. The fat elimination test is described under see section 4.2 posology and method of administration. In most cases, the plasma is already quite clear twelve hours after complete infusion of 2 g fat/kg body weight, equivalent to 20 ml Lipovenoes 10 % PLR/kg body weight. Liver function tests should also be carried out. If these show a clearly impaired liver function,

treatments should be discontinued.

This product contains soya-bean oil and egg phospholipids which may rarely cause allergic reactions. Cross allergic reaction has been observed between soya-bean oil and peanut. (See section 4.3). Patients with known allergy to soy or egg protein should not be given Lipovenoes 10 % PLR until hypersensitivity tests have been conducted and potential allergy has been excluded.

Lipovenoes 10 % PLR should be used with caution in patients with pulmonary disease, sepsis or any other condition with an intense inflammatory component. If administration is considered in such patients, the elimination of fat should be monitored daily.
Safety of prolonged Lipovenoes 10 % PLR therapy in patients receiving heparin and other anticoagulants or suffering from coagulation disorders has not been established.
Because free fatty acids are known to displace bilirubin from albumin binding sites, the use of lipid infusions in jaundiced or premature infants should be undertaken with caution.

The application of Lipovenoes 10 % PLR in pediatric patients with hyperbilirubinaemia has to be monitored carefully (risk/benefit). Bilirubin has to be checked closely when administering a fat emulsion due to the risk of kernicterus.

Light exposure of solutions for intravenous parenteral nutrition, especially after admixture with trace elements and/or vitamins, may have adverse effects on clinical outcome in neonates, due to generation of peroxides and other degradation products. When used in neonates and children below 2 years, Lipovenoes 10 % PLR should be protected from ambient light until administration is completed (see sections 4.2, 6.3 and 6.6).

4.5 Interaction with other medicines and other forms of interaction

Incompatibilities may occur through the addition of polyvalent cations (e.g. calcium), especially with the use of heparin.

Lipovenoes 10 % PLR should only be mixed with other infusion solutions, electrolyte concentrates or medicines when the compatibility has been proven.

4.6 Fertility, pregnancy and lactation

Lipovenoes 10% PLR should not be used in the first trimester of the pregnancy (see section 4.3 “Contraindications”). Because of the lack of specific experiences. Lipovenoes 10% PLR should only be used during the remaining period of pregnancy and lactation after a careful benefit/risk evaluation.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

The following possible early reactions with the administration of fat emulsions have been reported and the frequencies are unknown:

Vascular disorders:

Priapism (very rare cases)

Respiratory, thoracic and mediastinal disorders:

Shortness of breath

Gastrointestinal disorders:

Nausea, vomiting, lack of appetite

Skin and subcutaneous tissue disorders:

Pigmentation of tissues may occur after prolonged therapy with fat emulsions

Musculoskeletal, connective tissue and bone disorders:

Pains in the head, back, bones, chest and loins

General disorders and administration site conditions:

Slight rise in temperature (fever and chills)

Heat/cold sensation

Abnormal feeling of warmth (flush) or blueness (cyanosis)

Investigations:

Increased levels of transaminases, alkaline phosphatases and bilirubin have been observed after 6 to 8 weeks of infusion.

Should these side effects occur or the triglyceride level under infusion of fat rise above a value of 3 mmol/l in adults and 1,7 mmol/l in children, the fat infusion should be stopped or, if necessary, continued at a reduced dosage.

The prolonged infusion of soybean oil emulsion or its administration to patients with impaired liver metabolism has been associated with the “overload syndrome”, which exhibits the following symptoms, with frequencies unknown:

Blood and lymphatic system disorders:

Bone marrow depression

Anaemia

Thrombocytopenia

Leucopenia

Spontaneous bleeding

A change or reduction of some coagulation factors, (e.g. bleeding time, coagulation time, prothrombin time, thrombocyte count)

Hepatobiliary disorders:

Hepatosplenomegaly

Enlargement of the liver (hepatomegaly) with or without jaundice (icterus)

Pathological liver function tests.

Investigations:

Hyperlipidaemia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

The symptoms of overdosage are those described for the overload syndrome under see section 4.8 undesirable effects.

Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 25.2 Other nutrients

Lipovenoes 10 % PLR is a fat emulsion for intravenous nutrition, containing refined soybean oil emulsified with fractionated egg lecithin, supplying energy and essential fatty acids. No pharmacological, as opposed to nutritional, effects have been noted in man.

The main fatty acid is linoleic acid. The fat particles are similar in size and composition (excluding apoprotein) to chylomicrons.

The energy content of Lipovenoes 10 % PLR is about 4 522 kJ/l (1 080 kcal/l).

The theoretic osmolarity is 272 mosm/l, and the pH value 6,5 - 8,7.

5.2 Pharmacokinetic properties

Not Applicable

5.3 Preclinical safety data

Not Applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Inactive ingredients:

Sodium oleate, sodium hydroxide, water for injection.

6.2 Incompatibilities

Incompatibilities may occur through the addition of polyvalent cations (e.g. calcium), especially with the use of heparin.

Lipovenoes 10 % PLR should only be mixed with other infusion solutions, electrolyte concentrates or medicines when the compatibility has been proven.

6.3 Shelf life

24 months

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed (see sections 4.2, 4.4 and 6.6).

6.4 Special precautions for storage

Store at or below 25 °C. Do not freeze. Protect from light.

6.5 Nature and contents of container

Infusion bottles containing 100 ml, 250 ml, and 500 ml.

(Hospital packs available containing 10 infusion bottles).

The container closure system consists of a glass bottle which is closed with an elastomeric stopper.

6.6 Special precautions for disposal and other handling

Shake before use. Use only if the emulsion is homogenous and the container is undamaged. To be used immediately after opening the bottle. Any emulsion for infusion remaining after infusion must be discarded.

Fat emulsions should not be mixed with other medicinal products, except for parenteral nutrition products for which compatibility has been documented. When mixing with other nutrients like electrolytes, vitamins or trace elements to Lipovenoes 10% PLR for complete parenteral nutrition, care should be given to aseptic techniques, thorough mixing and, in particular, to compatibility. Under no circumstances Lipovenoes 10% PLR should be stored after addition of other components. Unless no other stability data are available, admixtures should be used within 24 hours.

When used in neonates and children below 2 years, protect from light exposure, until administration is completed. Exposure of Lipovenoes 10% PLR to ambient light, especially after admixture with trace elements and/ or vitamins, generates peroxides and other degradation products that can be reduced by protection from light exposure (see sections 4.2, 4.4 and 6.3).

7 HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi South Africa (Pty) Limited

Stand 7, Growthpoint Park

162 Tonneti Street

Halfway House, Extension 7

1682

8 REGISTRATION NUMBER(S)

29/25.2/0613

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15 April 1997

10 DATE OF REVISION OF THE TEXT

23 July 2021

Namibia NS2 04/25.2/1036