Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pedismof emulsion for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Pedismof consists of a three chamber bag system. Each bag, two different bag sizes, contains the following partial volumes:

	1000 ml	**1500 ml**
Amino acid solution 6.5% with electrolytes	319 ml	479 ml
Glucose 18.2%	573 ml	859 ml
Lipid emulsion 20 %(SMOFlipid)	108 ml	162 ml

If lipid administration is undesirable, the design of the bag allows the possibility to activate only the peel seal between the amino acids/electrolytes and glucose chambers, leaving the peel seal between the amino acids and lipid chambers intact. The content of the bag can subsequently be infused with or without lipids. The composition of the drug product after activation, i.e. mixing of the two (amino acids and glucose, two chamber bag, 892 mL solution (1000 mL three chamber bag), 1338 mL solution (1500 mL three chamber bag)) or three (amino acids, glucose and lipid, three chamber bag, 1000 mL emulsion (1000 mL three chamber bag), 1500 mL emulsion (1500 mL three chamber bag)) chambers are provided in the following table.

After combining two or three chambers - this corresponds to the following total compositions:

Active ingredients (g)	**Activated two chamber bag**		**Activated three chamber bag**	
Volume (ml)	**892**	**1338**	**1000**	**1500**
Amino acid chamber				
L-Alanine	2.0	3.0	2.0	3.0
L-Arginine	1.3	2.0	1.3	2.0
L-Aspartic acid	1.3	2.0	1.3	2.0
L-Cysteine	0.32	0.48	0.32	0.48
L-Glutamic acid	2.3	3.4	2.3	3.4
Glycine	0.67	1.0	0.67	1.0
L-Histidine	0.67	1.0	0.67	1.0
L-Isoleucine	0.99	1.5	0.99	1.5
L-Leucine	2.2	3.4	2.2	3.4
Lysine monohydrate *corresponding to* L-Lysine	1.8	2.7	1.8	2.7
L-Methionine	0.42	0.62	0.42	0.62
L-Phenylalanine	0.86	1.3	0.86	1.3
L-Proline	1.8	2.7	1.8	2.7
L-Serine	1.2	1.8	1.2	1.8
Taurine	0.096	0.14	0.096	0.14
L-Threonine	1.2	1.7	1.2	1.7
L-Tryptophan	0.45	0.67	0.45	0.67
Tyrosin	0.16	0.24	0.16	0.24
L-Valine	1.2	1.7	1.2	1.7
Calcium gluconate monohydrate *corresponding to* Calcium gluconate	2.9	4.3	2.9	4.3
Sodium glycerophosphate (hydrate) *corresponding to* Sodium glycerophosphate	1.5	2.2	1.5	2.2
Magnesium sulphate heptahydrate *corresponding to*				

Magnesium sulphate	0.20	0.30	0.20	0.30
Potassium chloride	1.2	1.9	1.2	1.9
Sodium acetate trihydrate *corresponding to* Sodium acetate	0.40	0.59	0.40	0.59
Glucose chamber				
Glucose monohydrate *corresponding to* Glucose	104	156	104	156
Lipid chamber				
Soya-bean oil, refined	0	0	6.5	9.8
Medium-chain triglycerides	0	0	6.5	9.8
Olive oil, refined	0	0	5.4	8.1
Fish oil, rich in omega-3-acids	0	0	3.3	4.9

Corresponding to:

	Activated two chamber bag			**Activated three chamber bag**		
Per volume unit (ml)	**892**	**1338**	**100**	**1000**	**1500**	**100**
Amino acids (g)	21	31	2.3	21	31	2.1
Nitrogen (g)	3.3	5.0	0.37	3.3	5.0	0.33
Electrolytes (mmol)						
- sodium[1]	18	27	2.0	19	28	1.9
- potassium	17	25	1.9	17	25	1.7
- magnesium	1.7	2.5	0.19	1.7	2.5	0.17
- calcium	6.7	10	0.75	6.7	10	0.67
- phosphate[1]	6.7	10	0.75	8.3	13	0.83
- sulphate	1.7	2.5	0.19	1.7	2.5	0.17
- chloride	17	25	1.9	17	25	1.7
- acetate	9.0	14	1.0	9.0	14	0.90
Carbohydrates (g)						
- Glucose (anhydrous)	104	156	11.7	104	156	10.4
Lipids (g)	-	-	-	22	33	2.2
Energy content (kcal)						
- total (approx.)	500	750	56.1	718	1077	71.8
- non protein (approx.)	417	625	46.7	634	951	63.4
Osmolarity (approx.) [2]	940 mOsm/L	940 mOsm/L	940 mOsm/L	860 mOsm/L	860 mOsm/L	860 mOsm/L
pH	5.6	5.6	5.6	5.6	5.6	5.6

[1]Contribution from the lipid emulsion and the amino acid solution.
[2] Calculated theoretical value

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Emulsion for infusion.

Glucose and amino acid solutions are clear and colourless to slightly yellow and free from particles. The lipid emulsion is white and homogenous.

Three chamber bag:
Osmolality: approx. 981 mOsm/kg
Osmolarity: approx. 860 mOsm/L
pH (after mixing): 5.6

Two chamber bag:
Osmolality: approx. 1037 mOsm/kg
Osmolarity: approx. 940 mOsm/L – Calculated theoretical value
pH (after mixing): 5.6

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Pedismof is indicated for parenteral nutrition in term neonates, infants, children, and adolescents when oral or enteral nutrition is not possible, insufficient, or contraindicated.

4.2 Posology and method of administration

The dosage depends on energy expenditure, the patient's body weight, age, clinical status, and on the ability to metabolize the constituents of Pedismof, as well as on additional energy or macronutrients given orally/enterally.
In paediatric patients requiring parenteral nutrition, lipids are an integral part of parenteral nutrition.
As shown in Table 1, total macronutrient composition depends on the number of activated chambers. The activated 3-chamber bag (three chamber bag) contains lipids, amino acids, and glucose. The activated 2-chamber bag (two chamber bag) contains amino acids and glucose. The glucose chamber should never be administered alone.

Posology
In neonates, the recommended dosage is up to 120 mL/kg/d for the activated three chamber bag and up to 107 mL/kg/d for the activated two chamber bag. The dose can be increased gradually over the first days. The maximum recommended daily dosage of 120 mL/kg for the activated three chamber bag and 107 mL/kg for the activated two chamber bag should not be exceeded.

In infants, the recommended dosage is 80 to 100 mL/kg/d for the activated three chamber bag and 71 to 89 mL/kg/d for the activated two chamber bag. The dose can be increased gradually over the first days. The maximum recommended daily dosage of 100 mL/kg for the activated three chamber bag and 89 mL/kg for the activated two chamber bag should not be exceeded.

In children, the recommended dosage is 60 to 80 mL/kg/d for the activated three chamber bag and 54 to 71 mL/kg/d for the activated two chamber bag. The dose can be increased gradually over the first days. The maximum recommended daily dosage of 80 mL/kg for the activated three chamber bag and 71 mL/kg for the activated two chamber bag should not be exceeded.

In adolescents, the recommended dosage is 40 to 50 mL/kg/d for the activated three chamber bag and 36 to 45 mL/kg/d for the activated two chamber bag. The dose can be increased gradually over the first days. The maximum recommended daily dosage of 50 mL/kg for the activated three chamber bag and 45 mL/kg for the activated two chamber bag should not be exceeded.

Table 1 Overview of Recommended Dosage for Activated three chamber bag and two chamber bag (units/kg/d) by Component

	Term neonates		**Infants**		**Children**		**Adolescents**	
	three chamber bag	**two chamber bag**	**three chamber bag**	**two chamber bag**	**three chamber bag**	**two chamber bag**	**three chamber bag**	**two chamber bag**
Fluid (mL)	≤120	≤107	80-100	71-89	60-80	54-71	40-50	36-45
Lipids (g)	≤2.6	-	1.8-2.2	-	1.3-1.7	-	0.9-1.1	-
Amino Acids (g)*	≤2.5	≤2.5	1.7-2.1	1.7-2.1	1.3-1.7	1.3-1.7	0.8-1.0	0.8-1.0
Glucose (g)	≤12.5	≤12.5	8.3-10.4	8.3-10.4	6.3-8.3	6.3-8.3	4.2-5.2	4.2-5.2
Energy (kcal)	≤86	≤60	58-72	40-50	43-57	30-40	30-36	20-25
Electrolytes (mmol)								
Sodium	≤2.2	≤2.2	1.5-1.9	1.5-1.8	1.1-1.5	1.1-1.5	0.7-0.9	0.7-0.9
Potassium	≤2.0	≤2.0	1.3-1.7	1.3-1.7	1.0-1.3	1.0-1.3	0.7-0.8	0.7-0.8
Chloride	≤2.0	≤2.0	1.3-1.7	1.3-1.7	1.0-1.3	1.0-1.3	0.7-0.8	0.7-0.8
Calcium	≤0.8	≤0.8	0.5-0.7	0.5-0.7	0.4-0.5	0.4-0.5	0.3	0.3
Phosphate	≤1.0	≤0.8	0.6-0.8	0.5-0.7	0.5-0.7	0.4-0.5	0.4	0.3
Magnesium	≤0.2	≤0.2	0.1-0.2	0.1-0.2	0.1	0.1	0.1	0.1

* Dose-limiting component: total dosage must be within the recommended limit of amino acids

In neonates and infants, Pedismof should be infused continuously over 20 to 24 hours. Cyclic infusion (administration in less than 20 to24 hours) may be introduced in stable infants. In children and adolescents, the infusion should be preferably 10 to 12 hours as cyclic infusion. The same bag should not be infused for longer than 24 hours.

Method of administration
Pedismof is for intravenous infusion into a central vein.

The recommended maximum infusion rate for the activated three chamber bag and two chamber bag are shown for neonates and infants in Table 2 and for children and adolescents in Table 3. The infusion rate is determined by dividing the volume by the duration of the infusion.
The infusion rate should be controlled using an electronic flow-regulating device (pump, syringe driver).

Table 2 Recommended Maximum Infusion Rate over 20 Hours for Activated three chamber bag and two chamber bag in Neonates and Infants (units/kg/h) by Component

	Activated three chamber bag		**Activated two chamber bag**	
	Term neonates	**Infants**	**Term neonates**	**Infants**
Fluid (mL)	6.0	5.0	5.35	4.45
Lipids (g)	0.13	0.11	-	-
Amino Acids (g)*	0.13	0.11	0.13	0.11
Glucose (g)	0.63	0.52	0.63	0.52

* Rate-limiting component: maximum rate must not exceed recommended rate of amino acids

Table 3 Recommended Maximum Infusion Rate over 10 Hours for Activated three chamber bag and two chamber bag in Children and Adolescents (units/kg/h) by component

	Activated three chamber bag		**Activated two chamber bag**	
	Children	**Adolescents**	**Children**	**Adolescents**
Fluid (mL)	8.00	5.00	7.10	4.50
Lipids (g)	0.17	0.11	-	-
Amino Acids (g)	0.17	0.10	0.17	0.10
Glucose (g)	0.83	0.52	0.83	0.52

* Rate-limiting component: maximum rate must not exceed recommended rate of amino acids

Treatment with parenteral nutrition may be continued for as long as is required by the patient's clinical conditions.

Vitamins, trace elements, and additional electrolytes can be added according to the physician's judgment if compatibility is confirmed and according to the clinical needs of the patient, see Section 6.6. Upon admixing vitamins, trace elements, or other additives, the final osmolarity of the mixture must be considered before selecting the route of infusion. For osmolarity calculations, see Section 6.6

When used in neonates and infants 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 instructions on preparation of the medicinal product before administration, see Section 6.6.

4.3 Contraindications

Hypersensitivity to egg, fish, soybean, peanut protein, or any of the active substances and excipients listed in Section 6.1.

In addition, all below listed contraindications apply when used as activated 3 chamber bag. When used as activated 2 chamber bag, i.e., without lipids, only those contraindications related to amino acids, electrolytes and glucose apply.

Amino acids:

- Congenital abnormality of the amino acid metabolism

Glucose:

- Severe hyperglycaemia

Lipids:

- Severe hyperlipidaemia or severe disorders of lipid metabolism characterized by hypertriglyceridemia

Electrolytes:

- Pathologically elevated plasma concentrations of electrolytes.

Concomitant treatment with ceftriaxone is contraindicated up to the age of 28 days, even if separate infusion lines are used (see section 4.5)

4.4 Special warnings and precautions for use

Hypersensitivity reactions
If any signs or symptoms of an anaphylactic reaction (such as fever, shiver, sweating, rash, or dyspnoea) occur, the infusion of Pedismof must be stopped immediately.

Infection
Since an increased risk of infection is associated with use of intravenous catheters, strict aseptic precautions must be taken in order to avoid any contamination during catheter insertion and manipulation.
Careful symptomatic and laboratory monitoring for fever, chills, leukocytosis, hyperglycaemia, and observation of catheter insertion site can help recognize early infections.

Refeeding syndrome
Administering PN to severely malnourished patients may result in refeeding syndrome, which is characterized by the intracellular shift of potassium, phosphorus, and magnesium as patients become anabolic. Thiamine deficiency and fluid retention may also develop. To prevent these complications, careful and slow initiation of PN is recommended with close monitoring of fluids and electrolytes.

Fat overload syndrome
In the event of fat overload syndrome, the infusion of Pedismof must be stopped immediately (see Sections 4.8 and 4.9).

Hyperglycaemia
In the event of hyperglycaemia, the infusion rate of Pedismof must be adjusted and/or insulin administered (see Sections 4.8 and 4.9).

Vitamin E / Tocopherol
Soya-bean oil, medium-chain triglycerides, olive oil, and fish oil naturally contain varying amounts of vitamin E (tocopherol). Also added is all-rac-α-tocopherol (another form of vitamin E) to limit lipid peroxidation.
When Pedismof is used as a 3-chamber bag, the content of alpha-tocopherol in the activated 3-chamber bag is 2.9 – 4.1 mg per 250 mL and 11.4 – 16.4 mg per 1000 mL. When Pedismof is used as 2-chamber-bag (without activated lipid compartment), no vitamin E (tocopherol) is contained.

Extravasation
Extravasation may occur in all intravenous infusions. The catheter insertion site should be evaluated daily for local signs of extravasation.

Light protection
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 of age, Pedismof should be protected from ambient light until administration is completed (see Sections 4.2, 6.3 and 6.6).

Monitoring/laboratory tests

Throughout treatment, monitor fluid and electrolyte status, acid-base balance, serum osmolarity, serum triglycerides, blood glucose, liver and kidney function, coagulation parameters, and complete blood count including platelets.

The lipids contained in Pedismof may interfere with some laboratory blood tests (e.g., haemoglobin, bilirubin, lactate dehydrogenase, and oxygen saturation) if blood is sampled before lipids have cleared from the bloodstream. Conduct these blood tests at least 4 to 6 hours after stopping the infusion.

Patients with renal impairment
Use with caution in patients with renal insufficiency. Fluid and electrolyte status should be closely monitored in these patients. Severe water and electrolyte disorders, severe fluid overload states, and severe metabolic disorders should be corrected before starting the infusion of Pedismof.

Patients with cardiovascular disorders
Use with caution in patients with pulmonary oedema or heart failure. Fluid status should be closely monitored.

Patients with hepatobiliary disorders
Use with caution in patients with severe liver insufficiency or elevated liver enzymes. Liver function parameters should be closely monitored.

Patients with unstable conditions
In case of unstable conditions (e.g., following severe post-traumatic conditions, decompensated diabetes mellitus, acute phase of circulatory shock, acute myocardial infarction, severe metabolic acidosis, severe sepsis, and hyperosmolar coma), the infusion of Pedismof should be monitored and adjusted to meet the clinical needs of the patient.

Compatibility
No additions to the bag should be made unless compatibility is confirmed (see Sections 6.2 and 6.6).

4.5 Interaction with other medicinal products and other forms of interaction

No pharmacodynamic interaction studies have been performed with Pedismof.

As for other calcium-containing infusion solutions, concomitant treatment with ceftriaxone and Pedismof is contraindicated in newborns (≤28 days of age), even if separate infusion lines are used due to the risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream. In patients older than 28 days, ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, including Pedismof, through the same infusion line (e.g., via Y-connector).
If the same infusion line is used for sequential administration, the line must be flushed thoroughly with a compatible fluid (e.g., physiological salt solution) to avoid precipitation.

Pedismof should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination.

Olive and soybean oil have a natural content of vitamin K1 that may counteract the anticoagulant activity of coumarin (or coumarin derivatives including warfarin).

4.6 Fertility, pregnancy and lactation

There are no data from the use of Pedismof in pregnant or breast-feeding women. Animal studies are insufficient with respect to reproduction toxicity. Pedismof can be used during pregnancy and breast-feeding if clearly indicated. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing Pedismof.

Fertility
No data are available. Effects on fertility are unlikely

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The pooled data from clinical trials and the postmarketing experience with individual macronutrient products (amino acids, lipids, glucose) in the paediatric population indicate the following adverse drug reactions (ADRs) may also occur under Pedismof treatment.

System organ class	Preferred MedDRA term	Frequency[a]
Hepatobiliary disorders	Cholestasis	Uncommon
	Hyperbilirubinaemia	Not known
Metabolism and nutrition disorders	Hypertriglyceridaemia	Common
	Hyperglycaemia	Common
	Hyperlipidaemia	Uncommon
General disorders and administration site conditions	Pyrexia	Uncommon

a) Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1 000 to <1/100); Rare (≥1/10 000 to <1/1 000); Very Rare (<1/10 000); Not known (cannot be estimated from the available data)

The following adverse reactions have been reported with other parenteral nutrition admixtures. Should these side-effects occur the infusion of Pedismof should be stopped or, if necessary, continued at a reduced rate/dosage.

Fat overload syndrome
Fat overload syndrome is a rare condition that has been reported with intravenous lipid injectable emulsions and is characterized by a sudden deterioration in the patient's condition (e.g., fever, anaemia, leukopenia, thrombocytopenia, coagulation disorders, hyperlipidaemia, hepatomegaly, deteriorating liver function, and central nervous system manifestations such as coma). A reduced or limited ability to metabolize lipids contained in Pedismof, accompanied by prolonged plasma clearance (resulting in higher lipid levels), may result in this syndrome. Although fat overload syndrome has been most frequently observed when the recommended lipid dose or infusion rate was exceeded, cases have also been described when the lipid formulation was administered according to instructions. The symptoms are usually reversible when the infusion of the lipid emulsion is stopped.

Excess of amino acid infusion
As with other amino acid solutions, the amino acid content in Pedismof may cause undesirable effects when the recommended infusion rate is exceeded. These effects are nausea, vomiting, shivering, and sweating. Amino acid infusion may also cause a rise in body temperature. With an impaired renal function, increased levels of nitrogen containing metabolites (e.g., creatinine and urea) may occur.

Excess of glucose infusion
If the glucose clearance capacity of the patient is exceeded, hyperglycaemia, glucosuria, and hyperosmolar syndrome may develop.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie;
E-mail: medsafety@hpra.ie.

4.9 Overdose

Adherence to dosing recommendations outlined Section 4.2 is essential to avoid overdose or mixing errors (see also Section 6.6) when handling small volumes. Close monitoring of biochemical parameters is essential to discover medication errors, i.e., overdose.

In the event of an overdose, fluid overload, electrolyte imbalance, fat overload syndrome, hyperglycaemia, or other adverse events may occur (see section 4.8), including e.g., nausea, vomiting, and shivering. The infusion must be stopped immediately.

There is no specific antidote, however, signs and symptoms of overdose are usually reversible after infusion is stopped. If symptoms persist after discontinuing infusion, diuresis, haemodialysis, hemofiltration may be indicated necessary. Further therapeutic measures depend on the particular symptoms and their severity.

When infusion is recommenced after the symptoms have declined, it is recommended that the infusion rate be raised gradually with monitoring at frequent intervals.

Close monitoring of biochemical parameters is essential to discover medication errors, i.e., overdose, and to treat all abnormalities appropriately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solutions for parenteral nutrition/combination, ATC code: B05BA10

The amino acid solution in Pedismof is containing all essential and the semi-essential amino acids (i.e., arginine, cysteine, glycine, proline, and tyrosine, as well as taurine) for neonates.
Amino acids are primarily used for protein synthesis, also serve as precursors for numerous biochemical pathways, and are important components of various signalling molecules. Specifically, taurine is important in the stabilisation of membrane potential, bile salt formation, growth, brain maturation, and development of the retina.

Glucose is the carbohydrate source in Pedismof.
It is important for neonates as primary source of energy because it can be used directly without enzymatic conversion, and it is an obligate energy source for brain metabolism.

The lipid emulsion included in Pedismof is SMOFlipid 20%, a mixture of soybean oil, medium-chain triglycerides, olive oil, and fish oil.
It provides fatty acids in the form of triglycerides which are hydrolysed by lipoprotein lipase to release free fatty acids. Fatty acids serve as a source of energy in form of triglycerides, structural components of cell membranes and tissues in form of phospholipids and glycolipids, and secondary messengers and mediators.

Soybean oil has a high content of polyunsaturated fatty acids, consisting mainly of the 2 essential fatty acids linoleic acid (LA, an omega-6 fatty acid) and alpha-linolenic acid (ALA, an omega-3 fatty acid).
Medium-chain triglycerides contain medium-chain fatty acids which are rapidly oxidised and provide the body with immediately available energy.
Olive oil is rich in the mono-unsaturated fatty acid oleic acid (an omega-9 fatty acid).
Fish oil is rich in the very-long-chain omega-3 polyunsaturated fatty acids (PUFAs), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and contains the very-long-chain omega-6 fatty acid arachidonic acid (AA). AA, EPA, and DHA are precursors of eicosanoids such as prostaglandins, thromboxanes, and leukotrienes. Although preterm neonates are capable of synthesizing AA from LA and DHA from ALA, the conversion is extremely limited. DHA and AA are important for brain development and normal body growth. The main accumulation of DHA in the brain and nervous tissue takes place during the last trimester of pregnancy and in the retina from gestational week 24 until birth. EPA is the primary precursor of the very-long-chain fatty acids (C24-C36) synthesized in the retina.

The mixed 4 oil lipid emulsion contains the essential fatty acids LA with a typical concentration of about 35 mg/mL (range of 28 to 50 mg/mL) and ALA with a typical concentration of about 5 mg/mL (range of 3 to 7 mg/mL), as well as the very-long-chain PUFA derived from fish oil EPA with a typical concentration of about 5 mg/mL (range of 2 to 7 mg/mL) and DHA with a typical concentration of about 4 mg/mL (range of 2 to 7 mg/mL).

All-rac-alpha-tocopherol in the lipid emulsion protects unsaturated fatty acids against lipid peroxidation and oxidative stress.

In published studies with SMOFlipid, the fatty acid profile in paediatric patients receiving the lipid emulsion revealed an increase in omega-3 fatty acids in plasma lipoproteins and red blood cell phospholipids and hence reflects the composition of the infused lipid emulsion. Arachidonic acid concentrations in plasma phospholipids were comparable between SMOFlipid and a standard soybean oil emulsion in premature neonates. There were comparable increases in body weight in both groups. There was no sign of clinical or biochemical evidence of essential fatty acid deficiency in any of the patients studied.

5.2 Pharmacokinetic properties

The amino acids, lipids, and glucose in Pedismof are distributed, metabolized, and eliminated in a similar manner as nutrients from oral or enteral nutrition.

Pedismof is infused intravenously resulting in bioavailability of 100%.

5.3 Preclinical safety data

There are no preclinical data of relevance to the safety evaluation beyond those already included in the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients	Amino Acid Chamber	Glucose Chamber	Lipid Chamber
all-*rac*- α -Tocopherol (E307)	-	-	X
Glacial acetic acid * (E260)	X	-	-
Glycerol (E422)	-	-	X
Purified Egg phospholipids	-	-	X
Sodium Hydroxide* (E524)	-	-	X
Sodium oleate	-	-	X
Water for injection	X	X	X

* for pH adjustment

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6

6.3 Shelf life

Shelf life of the medicinal product as packaged for sale
2 years

Shelf life after mixing the chambers of the bag
In-use stability of the mixed two and three chamber bags has been demonstrated for up to 7 days at 2-8°C followed by 48 hours at room temperature (20-25°C), including duration of administration. From a microbiological point of view the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless mixing has taken place in controlled and validated aseptic conditions.

Shelf life after mixing with additives
In-use stability of the mixed two and three chamber bags with additives (see section 6.6) has been demonstrated for up to 7 days at 2-8°C followed by either 48 hours at room temperature (20-25°C) or for 24 hours at 37 ± 2°C, including duration of administration. From a microbiological point of view, the product should be used immediately when additions have been made. If not used immediately, the in-use storage time and conditions prior to use are the responsibility of the user and should normally not be longer than 24 hours at 2-8°C, unless addition of supplements has taken place in controlled and validated aseptic conditions.

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

Do not store above 25°C. Do not freeze. Store in overpouch.

Shelf life after mixing: See section 6.3.
Shelf life after mixing with compatible medicinal products: See section 6.3

6.5 Nature and contents of container

The container consists of a multichamber primary bag and a secondary oxygen barrier bag. The primary bag is separated into three chambers by peelable seals. An oxygen absorber is placed between the primary bag and the secondary oxygen barrier bag. Should the integrity of the secondary oxygen barrier bag be compromised unintentionally, the package is also fitted with an integrity indicator between the primary bag and the secondary oxygen barrier bag. The integrity indicator should be inspected before removing the secondary oxygen barrier bag. If the indicator is black, the secondary oxygen barrier bag is damaged and the product should be discarded.

The primary bag is made of a multilayer polymer film, Biofine, which consists of polypropylene and synthetic rubber. The infusion and additive ports are made of polypropylene and synthetic rubber equipped with synthetic polyisoprene stoppers. The blind port, which is only used during manufacturing, is made of polypropylene and synthetic rubber equipped with a synthetic polyisoprene stopper.

Pack sizes:
6 x 1000 ml
4 x 1500 ml

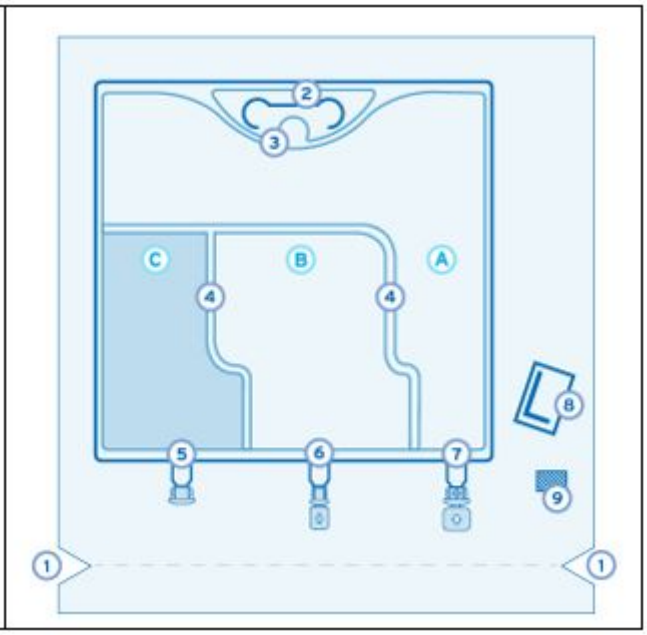
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use:
Do not use if package is damaged. Use only if the amino acid and glucose solutions are clear and colourless or slightly yellow and the lipid emulsion is white and homogenous. The contents of the two or three chambers have to be mixed before use, and before any additions are made via the additive port.

After separation of the peelable seals the bag should be inverted on a number of occasions to ensure a homogenous white emulsion mixture, which does not show any evidence of phase separation.

Schematic overview of the bag

1. Notches in the overpouch 2. Handle 3. Hole for hanging the bag 4. Peelable seals 5. Blind port (do not use this port) 6. Additive port (white) 7. Infusion port (blue) 8. Oxygen absorber* 9. Integrity indicator* *placed between the bag and the overpouch A. Glucose B. Amino acids C. Lipids	

1. Inspection of the bag

- The integrity indicator should be inspected before removing the overpouch. If the indicator is entirely black, the overpouch is damaged and the product should be discarded. If the indicator has any other colour than solid black, the product is safe to use.
- Use only if the amino acid and glucose solutions are clear and colourless or slightly yellow and the lipid emulsion is white and homogenous.

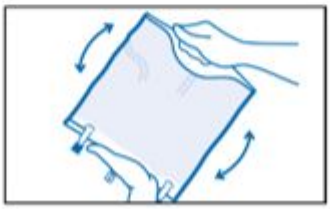
2. Removal of overpouch

• To remove overpouch, hold the bag horizontally and tear from the notch close to the ports along the upper edge.	
• Then simply tear the long side, pull off the overpouch and discard it along with the oxygen absorber and the integrity indicator.	

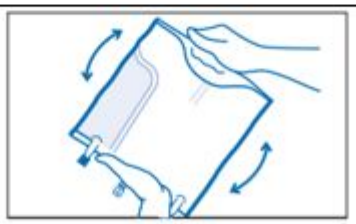
3. Mixing

The bag design allows for the activation of 3 chambers (lipids, amino acids, glucose) or 2 chambers (amino acids and glucose only) depending on the patient need.

3.1 Activation of the 3 chambers (mixing of 3 solutions by breaking two peelable seals)

• Place the bag on a clean, flat surface with text side up and ports pointing away from you.	
• Roll up the bag tightly from the handle side towards the ports, firstly with the right hand and then applying a constant pressure with the left hand until the vertical seals are broken.	
• The amino acids and glucose chambers should be mixed together before the lipid chamber. The vertical peel seals open due to the pressure of the fluid.	
• Mix the contents of the three chambers by inverting the bag three times until the components are thoroughly mixed (entire contents are white). *The liquids mix easily although the verticals seals remain partly closed.*	

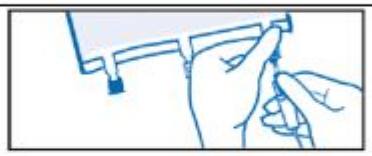
3.2 Activation of the 2 chambers (mixing of 2 solutions by breaking the peelable seal between the amino acid and glucose chamber)

• Place bag on a clean, flat surface with text side up and ports pointing away from you.	
• Roll up the bag tightly from the handle side towards the ports, firstly with the right hand and then applying a constant pressure with the left hand until the vertical seal between the amino acid and glucose chamber is broken. The vertical peel seals open due to the pressure of the fluid. *Do not apply pressure on the peelable seals next to the lipid chamber so that this chamber is not activated.*	
• Mix the contents of the two chambers by inverting the bag three times until the components are thoroughly mixed (a clear solution). *The liquids mix easily although the vertical seal remains partly closed.*	

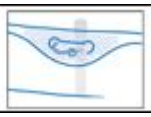
4. Additions (if prescribed)

• Place the bag on a flat surface again. Shortly before injecting additives, break off the white additive port cap with the arrow pointing toward the bag.	
• Hold the base of the additive port. Insert the needle through the centre of the additive port's septum and inject the additives (with known compatibility). • Mix thoroughly between each addition by inverting the bag three times. *The membrane of the additive port is sterile at first use. Use aseptic technique for the additions.*	

5. Finalising the preparation

• Immediately before inserting the infusion set, break off blue infusion port cap with the arrow pointing away from the bag.	
• Hold the base of the infusion port. Push the spike through the infusion port by rotating your wrist slightly until the spike is inserted. The spike should be fully inserted to secure it in place. *The membrane of the infusion port is sterile at first use.* *Use a non-vented infusion set or close the air-inlet on a vented set.*	

6. Hanging up the bag

• Hang the bag by the hole below the handle.	

Compatibility

Compatibility data are available with the named branded products Peditrace Novum, Vitalipid N Infant, Soluvit N and Glycophos in defined amounts, and generics of electrolytes in defined concentrations. When making electrolyte additions, the amounts already present in the bag should be taken into account to meet the clinical needs of the patient. Generated data supports additions to the activated bag according to the summary tables below:

Three chamber bag compatibility range stable for 7 days at 2-8°C followed by either 48 hours at room temperature (20-25°C) or for 24 hours at 37 ± 2°C

	Units	**Maximal total contents**	
Pedismof bag size	ml	1000	1500
Additive		**Volume**	
Peditrace Novum	ml	0 – 8.5	0 – 12.8
Soluvit N	vial	0 - 1	0 – 1.5
Vitalipid N Infant	ml	0 - 60	0 - 90
Electrolyte limits[1]			
Sodium	mmol/l	≤ 100	≤ 100
Potassium	mmol/l	≤ 100	≤ 100
Magnesium	mmol/l	≤ 5	≤ 5
Phosphate organic (Glycophos)	mmol/l	≤ 30	≤ 30

1. *includes amounts from all products*

Two chamber bag compatibility range stable for 7 days at 2-8°C followed by either 48 hours at room temperature (20-25°C) or for 24 hours at 37 ± 2°C

	Units	**Maximal total contents**	
Pedismof bag size, glucose and amino acid chambers only	ml	891.7	1337.5
Additive		**Volume**	
Peditrace Novum	ml	0 – 8.5	0 – 12.8
Soluvit N, reconstitued with water for injection	vial	0 – 0.9	0 – 1.4
Electrolyte limits[1]			
Sodium	mmol/l	≤ 100	≤ 100

Potassium	mmol/l	≤ 100	≤ 100
Magnesium	mmol/l	≤ 5	≤ 5
Phosphate organic (Glycophos)	mmol/l	≤ 30	≤ 30

1. *includes amounts from all products*

Note: These tables are intended to indicate compatibility. They are not a dosing guideline.
For branded products, before prescribing refer to national approved prescribing information.

Compatibility with further additives and the storage time of different admixtures will be available upon request.

If solutions are added to Pedismof, the osmolarity of the *final* mixture should be considered to choose the appropriate route of infusion (central or peripheral) (see also Section 4.2). The osmolarity can be calculated by summing up the products of osmolarity and volume for the individual solutions, divided by the sum of volumes of all solutions mixed (total volume in litre):

$$final\ Osm. = \frac{(Osm.\,Pedismof\ x\ Vol) + (Osm.\ Sol\ 1\ x\ Vol) + (Osm.\,Sol\ 2\ x\ Vol) + \cdots}{total\ Vol\ (Pedismof + Sol\ 1 + Sol\ 2 + \cdots)}$$

Osm. = osmolarity [milliosmols per litre, mOsm/L]
Vol = volume in litre [L]
Sol 1 = solution number 1 added
Sol 2 = solution number 2 added
… = further solutions to be added, if applicable
x = multiplied

Addition should be made aseptically.

For single use only. Any mixture remaining after infusion must be discarded.

Any unused medicinal product or waste material should be disposed in accordance with local requirement.

When used in neonates and children below 2 years, protect from light exposure, until administration is completed. Exposure of Pedismof 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 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1
Bad Homburg v.d.H 61352
Germany

8 MARKETING AUTHORISATION NUMBER

PA2059/087/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12th September 2025

10 DATE OF REVISION OF THE TEXT