Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

NUTRYELT, concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition of NUTRYELT expressed in quantities of salts per ampoule (10 ml) and per litre.

	Theoretical quantities of raw materials **expressed in anhydrous**	
NUTRYELT	For 1 ampoule (µg/10 ml)	For 1 litre (mg)
Zinc gluconate	69700	6970.0
Copper gluconate	2142.4	214.24
Manganese gluconate	445.69	44.569
Sodium fluoride	2099.5	209.95
Potassium iodide	170.06	17.006
Sodium selenite	153.32	15.332
Sodium molybdate	42.93	4.293
Chromium chloride	30.45	3.045
Ferrous gluconate	7988.2	798. 82

Content per ampoule of 10 ml

	NUTRYELT Molar composition (µmol /10 ml)	NUTRYELT Weight composition (µg /10 ml)
Zn	153	10000
Cu	4.7	300
Mn	1.0	55
F	50	950
I	1.0	130
Se	0.9	70
Mo	0.21	20
Cr	0.19	10
Fe	18	1000

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion

Clear, limpid and slightly yellow solution.

Density	1.0
pH	2.6 to 3.2
Osmolality	60 to 100 mosm/kg
Osmolarity	60 to 100 mosm/l

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

NUTRYELT is used as part of an intravenous nutrition regimen, to cover basal or moderately increased trace element requirements in parenteral nutrition.
NUTRYELT is indicated in adults only.

4.2. Posology and method of administration

Posology

For adults only.
The recommended daily dose in patients with basal to moderately increased requirements is one ampoule (10 ml) of NUTRYELT.
In cases of significantly increased trace element requirements (such as extensive burns, patients in severe hypercatabolic state due to major trauma) 2 ampoules (20 ml) of NUTRYELT may be given per day, and monitoring of serum trace element level is recommended.
In patients with renal, hepatic impairments or mild cholestasis the posology should be adapted (see section 4.4).

Paediatric population
NUTRYELT is contraindicated in children (see section 4.3).

Method of administration

NUTRYELT is not intended to be administered in its current presentation. It should be diluted according to the final desired osmolarity. The osmolarity value of the final preparation allows either administration through a peripheral vein, or only central venous catheter administration.

For incompatibilities and instructions for use see 6.2 and 6.6.

4.3. Contraindications

- Children
- Patients less than 40 kg body weight
- Pronounced cholestasis (serum bilirubin > 140 µmol/l)
- hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- in cases of Wilson's disease and hemochromatosis
- if serum concentrations of any of the trace elements contained in NUTRYELT are elevated.

4.4. Special warnings and precautions for use

The solution should be used after an accurate control of the patient clinical and biological parameters. Blood manganese levels should be regularly monitored in case of prolonged artificial nutrition: dose reduction may be necessary or NUTRYELT infusion should be stopped if manganese levels rise into the potentially toxic range (please refer to appropriate reference ranges).

Particular attention must be paid when the product is given to patients with reduced biliary excretion, since it could interfere with the biliary elimination of manganese, copper and zinc, leading to accumulation and overdose.
NUTRYELT should be used with caution in patients with impaired renal function as excretion of some trace elements (selenium, fluoride, chromium, molybdenum and zinc) may be significantly decreased.
In patients with renal, hepatic impairments or mild cholestasis the posology should be adapted.

In patients undergoing medium to long-term parenteral nutrition, there is an increased occurence of iron, zinc and selenium deficiency. In such circumstances, when necessary, the dosage should be adapted with the use of an extra supply of solutions, which contain only these individual components.

For patients receiving repeated blood transfusions, a risk of iron overload can occur.

Parenterally administered iron preparations can cause hypersensitivity reactions including serious and potentially fatal anaphylactic/anaphylactoid reactions. The risk is enhanced for patients with known allergies including drug allergies.

Chromium deficiency leads to a decrease in glucose tolerance, which improves after chromium supplementation. As a consequence, in diabetic patients on insulin medication, relative overdose of insulin and consecutive hypoglycemia may occur. Therefore controls of the blood glucose levels are recommended and re-adjustment of the insulin doses may become necessary.

NUTRYELT should be given with caution in cases of manifest hyperthyroidism or sensitivity to iodine if other iodine containing medicinal products (e.g. iodine antiseptics) are administered concomitantly.

This product contains 0.052 mmol of sodium (1.2 mg) per dose, i.e. essentially "sodium free".
This product contains 0.001 mmol of potassium (0.039 mg) per dose, i.e. essentially "potassium-free".

4.5. Interaction with other medicinal products and other forms of interaction

Combinations not recommended:

+ **Iron salts (oral route):**

Fainting or shock attributed to the rapid release of iron from its complex shape and transferrin saturation.

4.6. Fertility, pregnancy and lactation

Pregnancy
No safety data for NUTRYELT are available when it is administered during pregnancy. Therefore, NUTRYELT should not be used during pregnancy except after special consideration and if it is absolutely necessary.

Breast-feeding
No safety data for NUTRYELT are available when it is administered during lactation. Therefore, NUTRYELT should not be used during lactation except after special consideration and if it is absolutely necessary.

Fertility
No data available.

4.7. Effects on ability to drive and use machines

None stated.

4.8. Undesirable effects

The following adverse reaction(s) have been reported during post-marketing experience of trace elements solutions. The frequency is not known (cannot be estimated from the available data).

System organ class (SOC)	MedDRA Preferred Term
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Pain at the application site

Cases of hypersensitivity reactions including fatal anaphylactic reactions have been reported in patients receiving IV iron-containing products.

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 the national reporting system listed in Appendix V.

4.9. Overdose

If overdose is suspected, treatment with NUTRYELT should be withdrawn. Overdose should be confirmed by appropriate laboratory tests.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Electrolyte solutions
ATC code: B05XA31

NUTRYELT is a balanced solution composed of nine essential trace elements, which are necessary to maintain the metabolic equilibrium.
Trace elements are normally derived from a balanced diet, but the need increases in cases of insufficient supply or abnormal loss, hypercatabolism (surgery, major trauma, burns), and in cases of poor absorption (short bowel disease or Crohn's disease).
The composition of NUTRYELT is based on current International recommendations regarding the requirements for trace elements

During artificial nutrition, the supply of trace elements is necessary because a deficiency of any one of them can generate important metabolic and clinical disturbances.

5.2. Pharmacokinetic properties

The various pathways of trace element metabolism can be summarised as follows:
- Blood transport by proteins: albumin (Mn, Cu, Zn, Se), transferrin (Fe, Cr), ceruloplasmin (Cu), selenomethionine (Se), or non-protein carriers (F, I, Mo).
- Storage involving specific proteins: ferritin (Fe), thyroid hormones (I), selenoproteins (Se), or non-specific proteins: metallothioneins (Cu, Zn, Mn, Mo) or fluoroapatite (F).
- Elimination: The cationic trace elements (Fe, Cu, Mn, Zn) are eliminated mainly through biliary excretion. The anionic trace elements (I, F) and some oxygenated forms of minerals (Mo, Se, Cr) are primarily excreted in the urine.
  Elimination through the lungs and the skin is possible.

5.3. Preclinical safety data

Since trace element solutions for intravenous injection are well-known products that have been used for medical purposes for many decades, no preclinical studies have been specifically performed with NUTRYELT.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Hydrochloric acid (for pH adjustment)
- Water for Injections

6.2. Incompatibilities

- NUTRYELT must not be used as a vehicle for other drugs.
- NUTRYELT, as with other trace element solutions, cannot be added directly to inorganic phosphate (additive) solutions.
- Degradation of ascorbic acid in parenteral nutrition mix is accelerated by trace elements

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

6.3. Shelf life

2 years.
After dilution, chemical and physical in-use stability has been demonstrated for 48 h at 25°C protected from light.
From a microbiological point of view, the product should be used immediately after dilution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4. Special precautions for storage

Do not freeze
Keep the container in the outer carton in order to protect from light.

6.5. Nature and contents of container

10 ml solution in polypropylene ampoule in pack sizes of 10, 25 and 50.
Not all pack sizes may be marketed

6.6. Special precautions

Before use, check that the concentrate for solution for infusion is homogeneous and that the bottle is not damaged and is free of particles.
NUTRYELT is not intended to be administered in its current presentation. NUTRYELT must be diluted or mixed with gentle agitation during preparation under strict aseptic conditions, before infusion.
NUTRYELT must be diluted with respect to the final appropriate osmolarity. For example:

- 10 to 20 ml of NUTRYELT can be diluted in at least 250 ml of Sodium Chloride 0.9 % solution for infusion,
- 10 to 20 ml of NUTRYELT can be diluted in at least 250 ml of Glucose 5% solution for infusion

The pH after reconstitution of 20 ml of NUTRYELT with 250 ml Sodium chloride 0.9% will be 3.3, or 3.3-3.4 with Glucose 5%.

The reconstituted solution for infusion has to be visually inspected prior to use. Only clear solution without particles should be used.
Do not store partly used containers and discard all equipment after use.
The compatibility with solutions administered simultaneously via a common inlet cannula must be ensured.

7. MARKETING AUTHORISATION HOLDER

LABORATOIRE AGUETTANT
1 rue Alexander Fleming
69007 LYON
FRANCE

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.