SELENIUM AGUETTANT
concentrate for solution for infusion 10 micrograms/ml
Selenium

AGUETTANT

1. NAME OF THE MEDICINAL PRODUCT
SELENIUM AGUETTANT concentrate for solution for infusion 10 micrograms/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 10 ml vial contains 100 micrograms of selenium as sodium selenite (219 micrograms).
Each ml of solution contains 10 micrograms of selenium as sodium selenite (21.9 micrograms).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Concentrate for solution for infusion. Clear, colourless solution.
pH between 8.0 and 9.5.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
Selenium supplementation during parenteral nutrition.
Treatment of selenium deficiency which cannot be compensated by nutrition.

4.2. Posology and method of administration
Posology
1 ml of solution contains 10 micrograms of selenium.
The dose must be adjusted according to the needs of the patient.
The recommended dosage is:
Adults:
• Total parenteral nutrition: 60 to 100 micrograms daily.
• Selenium deficiency: 100 micrograms (up to a maximum of 400 micrograms) daily for a short period until normalisation of laboratory tests.
Paediatric population:
• Total parenteral nutrition:
  - Infants: 2 micrograms/kg/day and infants with low birth weight: 2 to 3 micrograms/kg/day.
  - Children: 2 to 3 micrograms/kg/day, up to a maximum of 30 micrograms daily.
  - Adolescents: no data are available.
• Selenium deficiency: no data are available
Selenium serum levels must be monitored regularly (every 6 to 12 months) in long-term parenteral nutrition and in case of renal impairment or more frequently in case of clinical signs of deficiency.
The dose must be adjusted to each individual as a function of the selenium deficiency and the selenium status.
Method of administration
Administration by intravenous route:
SELENIUM AGUETTANT concentrate for solution for infusion 10 micrograms/ml must be administered after dilution in solution for parenteral nutrition, after the stability has been validated, or in an isotonic solution (such as 0.9% sodium chloride or 5% glucose) with a slow infusion rate.

4.3. Contraindications
Hypersensitivity to the active substance

4.4. Special warnings and precautions for use
Special warnings:
This product must on no account be injected pure, but diluted in a solution for infusion (see section 4.2).
Precautions for use:
Serum selenium levels must be monitored regularly.
In case of complex parenteral nutrition protocols, precautions must be taken to avoid incompatibilities between the medicinal products added (see sections 6.2 and 6.6).
This medicinal product contains less than 1 mmol sodium (23 mg) of sodium per vial, that is to say essentially “sodium-free”.

4.5. Interaction with other medicinal products and other forms of interaction
No interaction studies have been performed.

4.6. Fertility, pregnancy and lactation
Pregnancy
There are no data from the use of selenium in pregnant women. The limited published data from studies performed in animals demonstrated a toxicity for reproduction at maternal toxic doses (see section 5.3.).
There are no safety data concerning the administration of SELENIUM AGUETTANT during pregnancy. Therefore, the use of SELENIUM AGUETTANT should only be used during pregnancy if required.
Lactation
Selenium is excreted in human milk. There are no safety data concerning the administration of SELENIUM AGUETTANT during lactation. Therefore, the use of SELENIUM AGUETTANT should only be used during lactation if required.
Fertility
There are no data on fertility from the use of selenium in humans. Selenium did not impair fertility in male rats, and effects on fertility in female rodents were only observed at very high doses (see section 5.3). Overall, the doses used to correct selenium deficiency are not expected to exert adverse effects on fertility.

4.7. Effects on ability to drive and use machines
SELENIUM AGUETTANT concentrate for solution for infusion 10 micrograms/ml has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects
The undesirable effects listed below have been observed during clinical studies and/or after marketing and are based on data from clinical trials and classified according to the MedDRA system organ class. The frequency categories are defined according to the following convention: 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), and not known (cannot be estimated from the available data).

System organ class	Not known Frequency
General disorders and administration site conditions	Inflammation at the infusion site

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.

4.9. Overdose
The symptoms of an acute overdose are: bad breath (garlic smell), tiredness, nausea and vomiting, diarrhoea and abdominal pain.
In case of chronic overdose, effects on the skin and its appendages which manifest themselves as a fragility and changes in the growth of nails and hairs, as well as peripheral polyneuropathies have been observed.
In case of overdose, the treatment must be interrupted, and a symptomatic treatment should be initiated if necessary.
There is no known specific antidote. In case of extreme overdose (1,000 - 10,000x), elimination of selenite by dialysis can be attempted.
In case of intoxication, selenium blood levels should be monitored at least once a month, until they return to a level that conforms with the recommendations.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Mineral supplements - ATC code: A12CE02.
Selenium is an essential trace element. In humans, selenium-containing compounds are glutathione peroxidase and a plasma selenium protein P found as selenocysteine. Glutathione-peroxidase is part of the antioxidant protection system of mammal cells.
Other selenium-dependent enzymes, thioredoxin-reductase and 5'-deiodinase, act as catalysts of the conversion of tetraiodothyronine (T4) into the active thyroid hormone triiodothyronine (T3).
On a patho-physiological level, the importance of selenium-dependent reactions has been demonstrated by observations in selenium deficiencies.
Selenium-containing glutathione-peroxidase modifies leucotriene, thromboxane and prostacyclin metabolism. Selenium deficiency inhibits immune system reactions, in particular cell-mediated and humoral non-specific responses. Selenium deficiency affects the activity of some hepatic enzymes.
Selenium deficiency potentiates oxidative or chemical liver damage as well as the toxicity of heavy metals, such as mercury and cadmium.
Selenium deficiency associated with clinical manifestations can also be caused by a long period of parenteral route nutrition or unbalanced diets.
Cardiomyopathies and myopathies are observed more frequently.

5.2. Pharmacokinetic properties
In the blood, selenite is mainly absorbed by erythrocytes and reduced to hydrogen selenide via enzymatic route. Hydrogen selenide serves as a central selenium pool for excretion and for specific incorporation in selenoproteins. In this reduced form, selenium is bound to proteins present in the liver and other organs. Plasma secondary transport from the liver to the target tissues that synthesise glutathione-peroxidase takes place in the selenocysteine form (selenoprotein P), which is then incorporated in the peptide chains of glutathione-peroxidase.
The total amount of selenium in the human body ranges between 3 and 20 mg. In humans, selenium is excreted in urine, faeces or through the lungs, depending on the dose administered. Selenium is primarily excreted by renal route as trimethylselenonium ion. Excretion depends on the selenium status.
The excretion of selenium administered by intravenous route or oral route takes place in three phases, the terminal half-life ranges from 65 to 116 days.

5.3. Preclinical safety data
Literature data on the single and repeated dose toxicity of selenium and sodium selenite does not reveal any toxic effects on health in addition to those already known from experience in humans. The target organs of the toxicity may be the lungs, nervous system and gastrointestinal tract. Reproduction toxicity was only observed at very high doses and there is no evidence of risk of teratogenic effects in mammals at non-toxic maternal doses. Even though the mutagenicity and carcinogenicity data are inconclusive given that there are both evidence of positive and negative effects, the adverse effects on these endpoints are generally observed at concentrations that are higher than the normal physiological levels.
According to the International Agency for Research on Cancer, selenium cannot be classified with respect to its carcinogenicity in humans.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Water for injections.

6.2. Incompatibilities
Selenium is generally incompatible with high concentrations of ascorbic acid (reduction of selenite to elemental selenium, insoluble and unavailable as a nutritional source of selenium).
This medicinal product must not be mixed with other medicinal products except those mentioned in sections 4.2 and 6.6.

6.3. Shelf life
3 years.
The physico-chemical stability of SELENIUM AGUETTANT concentrate for solution for infusion 10 micrograms/ml when diluted in glucose 5% or sodium chloride 0.9% was demonstrated during 48 hours at 25°C.
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 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4. Special precautions for storage
Store at or below 30°C.

6.5. Nature and contents of container
This medicinal product is packaged in vials made of colourless type I glass with a capacity of 10 ml. Vials are closed with a type I bromobutyl stopper and sealed by a flip-off cap. Box of 10 vials.

6.6. Special precautions for disposal and other handling
This medicinal product may be diluted in an isotonic solution such as 0.9% sodium chloride or 5% glucose, and should not be mixed with other medicinal products unless the compatibility and stability of the mixture have been demonstrated (see section 4.2. Posology and method of administration).
Each ml of Selenium concentrate should be diluted in at least 5 ml of isotonic solution.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. PRODUCT OWNER AND MANUFACTURER
Laboratoire AGUETTANT
1 rue Alexander Fleming
69007 LYON - France

8. DATE OF REVISION OF THE TEXT
August 2023