5.3. Preclinical safety data
No specific information on I.V toxicity of zinc gluconate is available; however the toxicity of orally administered zinc has been well studied using different salts.
Long-term feeding to rodents of very large amounts of zinc salts resulted in growth retardation, anaemia and metabolic effect.
The weight of evidence, from in vitro and in vivo tests, suggests that zinc is apparently neither a mutagen nor a carcinogen.
Reproduction studies have not been conducted with zinc gluconate.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Water for injections.

6.2. Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section 4.2.

6.3. Shelf life
30 months.
After dilution, chemical and physical in-use stability has been demonstrated for 24 hours at room temperature (15 to 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
Do not store above 30°C.
Do not freeze.
For storage conditions after dilution of the medicinal product, see section 6.3.

6.5. Nature and contents of container
10 ml solution in glass vial with an elastomer (bromobutyl) stopper fitted with an aluminium cover and crimped.
Box of 10 vials.

6.6. Special precautions for disposal
For single use only. Do not store partly used containers and discard all equipment after use.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. PRODUCT OWNER AND MANUFACTURER

Laboratoire Aguettant
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69007 Lyon
France

8. DATE OF REVISION OF THE TEXT

April 2023

106412

ZINC AGUETTANT
concentrate for solution for infusion 1 mg/mL

1. NAME OF THE MEDICINAL PRODUCT

ZINC AGUETTANT concentrate for solution for infusion 1 mg/mL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 6.97 mg of zinc gluconate, equivalent to 1 mg of zinc (i.e 15.29 micromoles).
Each vial of 10 ml contains 69.7 mg of zinc gluconate equivalent to 10 mg of zinc (i.e 152.9 micromoles).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion. Clear colourless solution.
Osmolarity: between 25 and 45 mosmol/l.
Osmolality: between 25 and 45 mosmol/kg.
Density: 1.006 g/cm3 (at 25°C).
pH: between 5.0 and 7.0.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications
Zinc supplementation solution in prolonged parenteral nutrition and in situations where a pronounced zinc deficiency may occur: e.g. severe malnutrition, hypercatabolism, digestive fistula, chronic diarrhoea.

4.2. Posology and method of administration
Posology
The dosage must be adapted to each patient, taking into account losses and zinc status.
The solution is a supplementation additive for parenteral nutrition intended to be used in compatible mixtures for parenteral nutrition or diluted in isotonic solutions.
Recommended basal requirements by intravenous route are the following. Higher doses may be needed to compensate abnormally high losses.
Adults:
• 2.5 to 5 mg/day.
Paediatric population:
• premature: 0.40 to 0.50 mg/kg/day,
• infants younger than 3 months: 0.25 mg/kg/day,
• infants older than 3 months: 0.1 mg/kg/day,
• children: 0.05 mg/kg/day to a maximum of 5 mg/day.
Method of administration
Recommended administration: intravenous route after dilution with a slow infusion rate.
The recommended administration is by intravenous route after dilution with a slow infusion rate.

The solution can be diluted in an isotonic solution (such as sodium chloride 0.9% or glucose 5%).
When removing a volume using a syringe, do not use a needle with a diameter greater than 0.8 mm.
Monitoring
Monitor zinc concentrations during treatment. Also monitor patients clinically for signs and symptoms of zinc deficiency, especially in pediatrics. Zinc concentrations may vary depending on the assay used and the laboratory reference range.

4.3. Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4. Special warnings and precautions for use
Warning
This product must not be given undiluted.
Precaution for use
In complex parenteral nutrition protocols, special precaution is required to avoid incompatibilities among the added medications.
Use in liver impairment
Zinc gluconate should be used with caution in case of impaired liver function, which may impair the biliary elimination of zinc leading to accumulation and overdose.
Use in renal impairment
Zinc gluconate should be used with caution in case of impaired renal function, as excretion of zinc may be significantly decreased.

4.5. Interaction with other medicinal products and other forms of interaction
Large doses of oral zinc inhibit copper absorption. Clinical significance of this interaction for intravenous zinc remains unclear.

4.6. Fertility, pregnancy and lactation
Pregnancy
Animal reproduction studies have not been conducted with zinc gluconate. It is not known whether zinc can cause foetal harm when administered to a pregnant woman, or whether it can affect reproductive capacity. Therefore, zinc gluconate injection should be administered to pregnant women only if clearly indicated.
Breast-feeding
Zinc is present in human milk. Administration of the approved recommended dose of Zinc gluconate injection in parenteral nutrition is not expected to cause harm to a breastfed infant. There is no information on the effects of Zinc gluconate on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Zinc gluconate injection and any potential adverse effects on the breastfed infant from Zinc gluconate injection or from the underlying maternal condition.
Fertility
No fertility data are available.

4.7. Effects on ability to drive and use machines
Not relevant.

4.8. Undesirable effects
Summary of the safety profile
Undesirable effects are mainly observed at high doses (see section 4.9).
Tabulated list of adverse reactions
General disorders and administration site conditions:
Infusion site inflammation (frequency not known).
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
Hyperamylasaemia without evidence of acute pancreatitis, nausea, vomiting, fever, anaemia, hypotension, pulmonary oedema, diarrhoea, jaundice, oliguria, cardiac arrhythmias and thrombocytopenia have been reported in patients with overdose.
Other manifestations of toxicity may include profuse sweating, blurred vision, decreased consciousness and hypothermia.
There is no known antidote for acute zinc toxicity. Management of zinc overdosage is supportive care based on presenting signs and symptoms.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties
Pharmacotherapeutic group: MINERAL SUPPLEMENTS; ATC code: A12CB02
Zinc has three main biological roles: catalytic, structural and regulatory.
Zinc is a component of many metalloenzymes including carbonic anhydrase, alkaline phosphatase, carboxypeptidase, oxidoreductases, transferases, ligases, hydrolases, isomerases and alcohol dehydrogenase.
Zinc is also involved in the structure and stabilisation of some enzymes, such as the antioxidant superoxide dismutase.
It also plays a role in the synthesis of RNA and DNA and in regulating the catabolism of RNA. Apoptosis is potentiated by zinc deficiency.
Zinc affects multiple aspects of the immune system.
Zinc is involved in some hormonal metabolisms (such as insulin, gustin, thymulin), and in the metabolism of carbohydrates, lipids and proteins.
It has an important place in the growth of premature babies, infants and children with increased requirements.
Zinc has an effect on tissue integrity and the sense of taste.
Considering all its potential biochemical activities, zinc is necessary for growth and cellular multiplication, in bone metabolism, immunity, reproduction. It contributes in protection against free radicals, inflammation and intervenes in cerebral functions. All these physiological actions can be modified by zinc deficiency.

5.2. Pharmacokinetic properties
Zinc is widely distributed in the body and is bound to albumin and metallothioneins. Zinc is mainly eliminated via the faecal route, resulting in increased elimination in chronic diarrhoea. Faecal excretion includes both unabsorbed dietary zinc and endogenous faecal zinc excretion.
Amino acids like histidine, threonine and lysine can bind zinc and promote its elimination via the kidneys.