APPROVED

Order of Ministry

of Health of Ukraine

**No. 290 dated 29.04.14**

Marketing Authorization

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**AMENDED**

**Order of the Ministry**

**of Health of Ukraine**

**No. 476 of 27.04.2017**

**INSTRUCTION**

for medical use of medicinal product

**Dialipon®**

Composition:

Active ingredient: thioctic acid;

Each mL of solution contains alpha-lipoic acid meglumine salt 58.382 mg equivalent to alpha-lipoic acid 30 mg on a 100% substance basis;

Excipients: meglumine (N-methylglucamine), polyethylene glycol 300 (Macrogol 300), water for injections.

Pharmaceutical form

Solution for infusions.

Basic physical and chemical properties: clear, yellow liquid.

Pharmacotherapeutic group

Alimentary tract and metabolism products. ATC Code А16А Х01.

Pharmacological properties

Pharmacodynamics

Thioctic acid is a vitamin-like substance naturally produced by the human body and acts as a coenzyme in oxidative decarboxylation of alpha-keto acids. Diabetic hyperglycaemia leads to vascular glucose accumulation in matrix proteins and formation of advanced glycation end products. This process causes decrease in endoneural blood flow and to endoneural hypoxia/ischemia. This is related to increased production of free oxygen radicals, which damage nerves and causes depletion of antioxidant glutathione in the peripheral nerves. In studies with rats thioctic acid was found to influence on the biochemical processes caused by streptozotocin-induced diabetes by decrease in the advanced glycation end products, improvement of endoneural blood flow, increase in physiological levels of glutathione in the affected diabetic nerve similar to the antioxidant action on free radicals. These effects observed through the studies show that the function of peripheral nerves could be improved by thioctic acid. This also concerns the sensory impairments in polyneuropathy manifested as dysesthesia, paraesthesia (burning, pain, numbness or tingling). The study of symptomatic treatment of diabetic polyneuropathy with thioctic acid proved beneficial effect of thioctic acid on the studied symptoms: paraesthesia, burning, tingling and pain.

Pharmacokinetics

Thioctic acid undergoes high first-pass hepatic metabolism. Systemic bioavailability significantly vary from patient to patient. Biotransformation of thioctic acid is by side chain oxidation and conjugation and 80-90% of its metabolites are excreted through the kidneys. The elimination half-life of thioctic acid is 25 minutes and the total plasma clearance is 10-15 mL/min/kg. After a 30-minute infusion of 600 mg thioctic acid its plasma concentration is approximately 20 µg/mL. Only small amounts of the intact substance are excreted with urine.

Clinical particulars

Indications

Paraesthesia in diabetic polyneuropathy.

Contraindications

Hypersensitivity to thioctic acid or to any of the excipients.

Interaction with other medicinal products and other forms of interaction

Thioctic acid react with ions complex metals (e.g. cisplatine), therefore the product may lower their effects.

Thioctic acid forms slightly soluble complexes with sugar molecules (e.g. levulose).

Thioctic acid is a metal chelator, so it can not be used together with metals (iron, magnesium).

Hypoglycaemic effect of antidiabetic drugs (insulin and/or others) could be increased. Therefore blood sugar levels should be strictly monitored, especially in the beginning of the therapy with thioctic acid. In single cases as prevention of hypoglycaemic syndromes, the insulin dosage or the dose of oral antidiabetic products might need to be reduced.

Special warnings and precautions for use

Diabetic patients need frequent blood glucose monitoring. In separate cases sugar-lowering agents shall be adjusted to prevent hypoglycaemia.

In treatment of polyneuropathy due to regenerative processes short-term increased sensitivity with paraesthesia and creeping sensation can develop.

Chronic use of alcohol is a risk factor of development of polyneuropathy and can decrease efficacy of Dialipon®. Therefore it is not recommended to drink alcohol during treatment.

The product is photosensitive therefore ampoules shall be taken from the carton just before use.

Intravenous thioctic acid should be restricted in elderly (over 75 years).

Use during pregnancy and lactation

Because of the lack of enough data of drug safety during pregnancy, the therapy should be taken only under medical supervision.

Because of lack of data for passing of thioctic acid in the mothers’ milk, the use of thioctic acid should be avoided during breast-feeding.

Effects on speed of reactions when driving or using machinery

During the period of treatment caution should be used in patients while driving and doing other potentially hazardous activities that require high concentration and rapid psychomotor reactions.

Posology and method of administration

The dose and duration of treatment should be determined by the physician individually.

10 mL to 20 mL intravenous dose daily equivalent to 300-600 mg of thioctic acid is recommended for intense paraesthesia. The solution for infusion should be used for 2-4 weeks in the initial stages of treatment. The product pre-dissolved in 250 mL of 0.9 % sodium chloride is administered intravenously. The infusion should be administered over at least 30 min. The active substance is sensitive to light exposure. The solution for infusion should be prepared immediately before administration and protected from light, for example, with aluminium foil. This reconstituted solution may be stored for up to 6 hours if protected from light.

Oral Dialipon® at a dose of 300-600 mg thioctic acid daily is used for the further therapy.

Paediatric population

Dialipon® is not recommended to be used in children and adolescents because of lack of studies in this category of patients.

Overdose

At overdose nausea, vomiting and headache are possible. It was reported that when administering 10 to 40 g thioctic acid in combination with alcohol, severe intoxication which can be lethal was observed. Clinical signs of intoxication were manifested as psychomotor disorders or fainting followed by generalized seizure and development of lactic acidosis. The result of intoxication is hypoglycaemia, shock, rhabdomyolysis, haemolysis, disseminated intravascular coagulation, bone marrow suppression and organ insufficiency.

Treatment. If severe intoxication with thioctic acid (more than 80 mg/kg thioctic acid of body mass) there should be immediate hospitalization and patients should be treated symptomatically as required (e.g. vomiting provocation, gastric lavage, intake of activated carbon). Treatment of generalized attacks, lactic acidosis and the other life threatening consequences of intoxication should be symptomatic and in compliance with the principles of modern intensive therapy. The use of haemodialysis and hemoperfusion and filtration in the process of forced elimination of thioctic acid isn’t still verified.

Undesirable effects

Nervous system disorders: taste distortion or dysgeusia, headache, flushing, increased sweating, shortness of breath, increased intracranial pressure, dizziness, cramps, blurred vision and double vision. In most cases all symptoms are self-localizing.

Gastrointestinal disorders: in fast intravenous injection nausea, vomiting, diarrhoea, abdominal pain, which are self-localizing.

Blood and lymphatic system disorders: petechial haemorrhage into mucosa, skin, thrombocyte disorders, hypocoagulation, haemorrhage rash (purpura), thrombophlebitis.

Metabolism and nutrition disorders: hypoglycaemia which may cause hypoglycaemia-like symptoms (dizziness, increased sweeting, headache, vision disorders) due to improved glucose disposal.

Immune system disorders: skin rash, urticaria, pruritus, eczema and systemic reactions up to anaphylactic shock.

Cardiac and vascular system disorders: in fast intravenous injection cardiac pain, tachycardia which are self-localizing.

Other: Injection site reactions, weakness.

Shelf life

5 years.

Do not use this medicine after the expiry date stated on the carton.

Storage

Store in the original package below 25 °С. Keep out of the reach of children.

Incompatibilities

Dialipon® react in vitro with ions complex metals (e.g. cisplatine), therefore the product may lower their effects. Dialipon® forms slightly soluble complexes with sugar therefore Dialipon® infusion solution is incompatible with glucose and fructose and Ringer’s solutions. The product is incompatible with solutions containing compounds which react with SH-groups or disulfide bridges. 0.9 % sodium chloride is used as a solvent.

Nature and contents of container

10 or 20 mL in an ampoule, 5 or 10 ampoules in a carton.

5 ampoules per blister; 1 or 2 blisters per carton.

Prescription status

Prescription only.

Manufacturer

JSC Farmak

Location

74, Frunze str., Kyiv, 04080.

Date of the last revision

27.04.2017.