APPROVED
Order of the Ministry of Health
of Ukraine No. _____
dated_____
Marketing Authorization
No._____

INSTRUCTION
for medical use of medicinal product

T-MEKSAT

Composition:
active substance: ethylmethylhydroxypyridine succinate;
1 ampoule (2 ml) of solution contains 100 mg of ethylmethylhydroxypyridine succinate;
excipients: sodium metabisulfite (E 223), water for injection.

Pharmaceutical form. Solution for injection.
Main physical and chemical properties: clear, colorless to slightly yellowish solution.

Pharmacotherapeutic group. Other nervous system drugs. ATC code: N07X X.

Pharmacological properties.
Pharmacodynamics.
T-MEKSAT is an inhibitor of the free radical processes and a membrane protector; it exerts the antihypoxic, stress-protective, nootropic, anticonvulsant and anxiolytic effects. The medicinal product increases the body's resistance to the effects of versatile hazard factors and to the oxygen-dependent pathological conditions (shock, hypoxia and ischemia, cerebrovascular accident, intoxication with alcohol and antipsychotic products [neuroleptics]).
T-MEKSAT improves the cerebral metabolism and blood supply to the brain, improves the microcirculation and rheological properties of blood, reduces the platelet aggregation. It stabilizes the membrane structures of blood cells (red blood cells and platelets) in the hemolysis. It exerts the hypolipidemic effect, reduces the level of total cholesterol and low-density lipoproteins (LDL). It reduces the enzymatic toxemia and endogenous intoxication in the acute pancreatitis.
The mechanism of action of the medicinal product is associated with its antihypoxic and membrane protective effects. It inhibits the lipid peroxidation, increases the superoxide dismutase activity, increases the lipid-protein ratio, reduces the membrane viscosity and increases its fluidity. It modulates the activity of the membrane-bound enzymes (calcium-independent phosphodiesterase, adenylate cyclase, acetylcholinesterase), receptor complexes (benzodiazepine, γ-aminobutyric acid [GABA], acetylcholine) enhancing their ligand-binding ability, facilitates preserving the structural and functional organization of biomembranes, transporting the neurotransmitters and improving the synaptic transmission. Ethylmethylhydroxypyridine succinate increases the brain dopamine levels. It causes the increased compensatory activity of the aerobic glycolysis and decreased inhibition rate of the oxidative processes in the Krebs cycle in the hypoxic conditions with the increased adenosine triphosphate (ATP) and creatine phosphate content, activation of the energy-synthesizing functions of mitochondria and stabilization of the cell membranes.
Ethylmethylhydroxypyridine succinate normalizes the metabolic processes in the ischemic myocardium, reduces the necrosis area, restores and improves the myocardial electrical activity and contractility and increases the coronary blood flow in the ischemic area, reduces the consequences of reperfusion syndrome in the acute coronary insufficiency. It increases the antianginal activity of nitro-products. Ethylmethylhydroxypyridine succinate promotes preserving the retinal ganglion cells and optic nerve fibers in the progressive neuropathy (the consequences of which are chronic ischemia and hypoxia). It improves the functional activity of the retina and optic nerve and increases the visual acuity.

Pharmacokinetics.
When administered intramuscularly, the medicinal product is detected in blood plasma within 4 hours after injection. The time to maximum concentration is 0.45–0.5 hour. When 400–500 mg doses are used, the maximum concentration is 3.5–4.0 μg/ml. T-MEKSAT rapidly passes from the bloodstream into the organs and tissues and is rapidly eliminated from the body. The medicinal product is excreted with urine, mainly as the glucuronic conjugates and in the insignificant amounts — in the unchanged form.

Clinical particulars.
Indications.
- acute cerebrovascular accidents;
- cranio-cerebral injury, consequences of the cranio-cerebral injuries;
- discirculatory encephalopathy;
- chronic cerebral ischemia;
- vegetative dystonia syndrome;
- mild (moderate) cognitive disorders;
- anxiety disorders in neurotic and neurosis-like conditions;
- acute myocardial infarction (from the first day) as part of the combination therapy;
- primary open-angle glaucoma of various stages, as part of the combination therapy;
- relief of withdrawal syndrome in alcoholism with predominant neurosis-like and neurocirculatory disorders;
- acute intoxication with antipsychotic drugs;
- acute purulent and inflammatory processes in the abdominal cavity (acute necrotizing pancreatitis, peritonitis), as part of the combination therapy.

Contraindications.
Acute hepatic or renal failure, individual hypersensitivity to the active substance and/or excipients of the medicinal product.
Pregnancy or lactation. Pediatric use.

Interaction with other medicinal products and other forms of interaction.
When used concomitantly, the medicinal product enhances the effect of benzodiazepine anxiolytics, anticonvulsants (carbamazepine) and antiparkinsonian products (levodopa). It reduces the toxic effects of ethyl alcohol. It increases the antianginal activity of nitro-products and antihypertensive activity of ACE and β-adrenergic blocking agents. Co-administration with nibentane, propranolol and verapamil reduces the risk of the arrhythmogenic effects of the latter ones; concomitant use with the neuroleptics reduces the risk of developing and severity of adverse reactions of the latter ones.

Special warnings and precautions for use.
In some cases, especially in the predisposed patients with bronchial asthma and with the increased sensitivity to sulfites, severe hypersensitivity reactions may develop. The medicinal product contains sodium metabisulfite that may cause the bronchospasm.
This medicinal product contains less than 1 mmol (23 mg)/dose of sodium, i.e. it is practically free of sodium.
T-MEKSAT should be used with caution in patients with the diabetic retinopathy (the course duration should not exceed 7–10 days) due to its property to potentiate the proliferative processes.
When the parenteral administration is completed, it is recommended to continue using the medicinal products in tablets orally to maintain the achieved effect.

Pregnancy and lactation.
Pregnancy. There is no data about using ethylmethylhydroxypyridine succinate in pregnant women. Animal reproductive toxicity studies do not demonstrate the direct or harmful effects. The medicinal product is contraindicated during pregnancy.
Lactation. It is not known whether ethylmethylhydroxypyridine succinate (metabolites) is (are) excreted in the milk of the breastfeeding woman. The medicinal product is contraindicated during breastfeeding.

Fertility. Animal reproductive toxicity studies do not indicate the reproductive toxicity.

Effects on ability to drive and use machines.
When the medicinal product is administered, caution should be exercised while performing the work that requires quick psychophysical reactions (driving vehicles, using machines, etc.).

Posology and method of administration.
The dosage regimen depends on the condition.
Intramuscular or intravenous (bolus injection or drop infusion) administration. When administered as infusion, the medicinal product should be diluted in 100–150 ml of 0.9% sodium chloride solution or 5% glucose solution. When T-MEKSAT is used as bolus injection, it should be administered slowly within 5–7 minutes; when it is used as drop infusion, the rate should be 40–60 drops per minute. The maximum daily dose should not exceed 1200 mg.
In the acute cerebrovascular accidents, T-MEKSAT is used in the first 10–14 days — 200–500 mg as intravenous infusion 2–4 times per day, then 200–250 mg intramuscularly 2–3 times a day for 14 days; after that it is recommended to switch to the oral dosage forms.
In the cranio-cerebral injury and consequences of the cranio-cerebral injuries, medicinal product T-MEKSAT is used within 10–15 days as intravenous infusion at 200–500 mg 2–4 times per day, after that it is recommended to switch to the oral dosage forms.
In the discirculatory encephalopathy in the decompensation phase, medicinal product T-MEKSAT should be used intravenously by bolus injection or drop infusion at 200–500 mg 1–2 times per day for 14 days. Then the medicinal product is administered intramuscularly at 100–250 mg daily for the next 2 weeks, after that it is recommended to switch to the oral dosage forms.
As the preventive course for discirculatory encephalopathy, the medicinal product is administered intramuscularly at 200–250 mg 2 times per day within 10–14 days, after that it is recommended to switch to the oral dosage forms.
In the chronic cerebral ischemia, the medicinal product is administered intravenously by drop infusion or bolus injection slowly at 10 ml (500 mg) once daily within 14 days, after that it is recommended to switch to the oral dosage forms.
In the mild (moderate) cognitive disorders, T-MEKSAT is administered intravenously by drop infusion or bolus injection slowly at 10 ml (500 mg) once daily within 14 days, after that it is recommended to switch to the oral dosage forms.
In anxiety disorders, the medicinal product is administered intramuscularly at daily dose of 100–300 mg/day within 14–30 days, after that it is recommended to switch to the oral dosage forms.
In the acute myocardial infarction, T-MEKSAT is administered intravenously or intramuscularly within 14 days secondary to the conventional therapy of the myocardial infarction involving nitrates, β-adrenergic blocking agents, ACE inhibitors, thrombolytics, anticoagulants and antiplatelets, as well as symptomatic agents as indicated. In the first 5 days, to achieve the maximum effect, it is advisable to administer the medicinal product T-MEKSAT intravenously; in the following 9 days, the medicinal product can be administered intramuscularly. Intravenous administration should be performed by drop infusion, slowly (to avoid the side effects) in 0.9% sodium chloride solution or 5% glucose solution in a volume of 100–150 ml within 30–90 minutes. Where appropriate, the medicinal product may be administered as the slow bolus injection (within at least 5 minutes).
T-MEKSAT is administered (intravenously or intramuscularly) 3 times per day every 8 hours. The daily therapeutic dose is 6–9 mg/kg of body weight per day, a single dose is 2–3 mg/kg of body weight. The maximum daily dose should not exceed 800 mg, a single dose — 250 mg.
In the open-angle glaucoma of various stages, T-MEKSAT is used as part of the combination therapy, intramuscularly at 100–300 mg/day, 1–3 times per day within 14 days.
In the alcohol withdrawal syndrome, T-MEKSAT is administered intravenously or intramuscularly at 200–500 mg 2–3 times per day within 5–7 days.
In the acute intoxication with antipsychotics, the medicinal product is administered intravenously at 200–500 mg/day within 7–14 days.
In the acute purulent and inflammatory processes in the abdominal cavity (acute necrotic pancreatitis, peritonitis), the medicinal product is prescribed on the first day both in the preoperative and

postoperative periods. The administered doses depend on the form and severity of the disease, process extent and the variants of the clinical course. The medicinal product should be discontinued gradually only after a stable positive clinical and laboratory effect.
In the acute edematous (interstitial) pancreatitis, medicinal product T-MEKSAT is administered at 200–500 mg 3 times per day by intravenous infusion (in isotonic sodium chloride solution) and intramuscular injection. *Mild necrotic pancreatitis*: 100–200 mg 3 times per day by intravenous infusion (in isotonic sodium chloride solution) and intramuscular injection. *Moderate form*: 200 mg 3 times per day by intravenous infusion (in isotonic sodium chloride solution). *Severe form*: as pulse dosing at 800 mg in the first day with a twice-daily dosage regimen, then 200–500 mg 2 times per day with the gradual tapering of daily dose. *Very severe form:* at initial dose of 800 mg/day until persistent relief of the pancreatogenic shock manifestations; when the condition is stabilized, at 300–500 mg 2 times per day by intravenous infusion (in isotonic sodium chloride solution) with the tapering of daily dose.
Elderly patients. No dose adjustment is required for the elderly patients.

Pediatric population. The medicinal product is contraindicated.

Overdose.
Symptoms: drowsiness, insomnia.
Treatment: due to the low toxicity, overdose is unlikely. Treatment is usually not required; symptoms disappear within a day. In the case of the marked manifestations, supportive and symptomatic treatment should be administered.

Undesirable effects.
To avoid the occurrence of the adverse reactions, it is recommended to follow the dosage regimen and the rate of the product administration. The frequency of the adverse reactions was determined based on the World Health Organization (WHO) classification: very common (≥ 10%); common (≥ 1% and ≤ 10%); uncommon (≥ 0.1% and ≤ 1%); rare (≥ 0.01% and ≤ 0.1%); very rare (≤ 0.01%); frequency not known (frequency cannot be estimated from the available data).
Immune system disorders: very rare — anaphylactic shock, angioedema, urticaria; frequency not known — allergic reactions, hyperemia, possible severe hypersensitivity reactions.
Psychiatric disorders: very rare — drowsiness; frequency not known — difficulties in falling asleep, anxiety, emotional reactivity.
Cardiovascular disorders: frequency not known — palpitations, tachycardia.
Nervous system disorders: very rare — headache, dizziness (may be associated with the extremely high rate of administration and be short-term); frequency not known — coordination impairment, tremor.
Vascular disorders: very rare — decreased/increased blood pressure (may be associated with the extremely high rate of administration and be short-term).
Respiratory, thoracic and mediastinal disorders: very rare — dry cough, throat irritation, chest discomfort, difficulty breathing (may be associated with the extremely high rate of administration and be short-term); frequency not known — bronchospasm.
Gastrointestinal disorders: very rare — dry mouth, nausea, unpleasant odor, metallic aftertaste; frequency not known — dyspeptic disorders, diarrhea.
Skin and subcutaneous tissue disorders: very rare — itching, rash, face hyperemia; frequency not known — distal hyperhidrosis.
General disorders and administration site conditions: very rare — warmth sensation; frequency not known — changes in the administration site.
In the long-term administration of the medicinal product, the following adverse reactions may occur: flatulence, weakness, peripheral edemas.
Reporting of suspected adverse reactions. Reporting of the suspected adverse reactions after authorization of the medicinal product is important. It allows the monitoring of the benefit/risk ratio of the medicinal product. Healthcare professionals, pharmaceutical specialists and patients or their legal representatives should report any suspected adverse reactions and lack of efficacy of the medicinal product via the automated pharmacovigilance information system at: https://aisf.dec.gov.ua.

Shelf life. 2 years.

Storage conditions.
Store in the original packaging, at temperature not exceeding 25 °C. Keep out of reach of children.

Incompatibility.
The medicinal product should not be mixed with other products. Use only solvents specified in the instruction.

Packaging. Each ampoule contains 2 ml; each blister contains 5 ampoules; each cardboard box contains 2 blisters.

Legal classification. By prescription.

Manufacturer. Private Joint Stock Company “Lekhim-Kharkiv”.

Address of manufacturer and place of its activity.
36 Severin Pototskyi St., Kharkiv, 61115, Ukraine.

Date of last review.