Mildronate®

International Non-Proprietary Name (INN): Meldonium

Dosage Form: solution for intramuscular, intravenous and parabulbar injection in ampoules/vials (5 ml)

Structure: 1 ml of the solution contains:
Active ingredient: Meldonium Dihydrate -100 mg;
Excipient: water for injections.

Description:
Transparent colorless liquid.

Pharmacological classification: metabolic means

ATC code: C01EB

Pharmacological action: antianginal, angioprotective, antihypoxic and cardioprotective.

Pharmacodynamics;
Meldonium is a synthetic analogue of gamma-butyrobetaine (GBB), a substance which exists in every cell of the human body. It inhibits gamma-butyrobetaine dioxygenase, reduces the synthesis of carnitine and transport of long-chain fatty acids through cell membranes, prevents the accumulation in cells of activated forms of unoxidized fatty acids (acylcarnitine and acyl-coenzyme A derivatives).
Under conditions of ischemia meldonium restores the equilibrium between the processes of oxygen delivery and its consumption in cells, prevents the violation of ATP (adenosine triphosphate) transport; simultaneously, it activates glycolysis, which proceeds without additional consumption of oxygen. As a result of carnitine concentration decrease, GBB (gamma-butyrobetaine) with vasodilating properties is intensively synthesized. The action mechanism determines the variety of pharmacological effects: increasing efficiency, reducing the symptoms of mental and physical overstrain, the activation of cell-mediated and humoral immunity, cardioprotective action. In the case of acute ischemic damage to the myocardium meldonium slows the formation of the necrotic zone, shortens the rehabilitation period. With heart failure increases myocardial contractility, increases physical activity tolerance, reduces the incidence of angina attacks. By acute and chronic ischemic disorders of cerebral circulation improves blood circulation in the ischemic focus and promotes redistribution of blood in favor of the ischemic site. Effective in the case of vascular and dystrophic pathology of the fundus vessels. Also there is a tonic effect on the central nervous system and the elimination of functional disorders of the somatic and autonomic nervous system for patients who suffer chronic alcoholism with the abstinence syndrome.
When it comes to increased physical activity, meldonium increases the body's resistance and the ability to restore energy reserves quickly, therefore Mildronate is used to enhance physical and mental performance.

Pharmacokinetics:
After intravenous introduction of the injection, the drug`s bioavailability is 100%. Maximum concentration (Cmax) in the blood plasma is achieved immediately. The compound is metabolized with the formation of 2 major metabolites, which are excreted by the kidneys. The half-life (T½) for intravenous introduction is 3-6 hours.

Intended uses:
In complex therapy of patients with coronary heart disease (angina, myocardial infarction, etc.); chronic heart failure and dyshormonal cardiomyopathy; in complex therapy of patients with acute and chronic cerebral circulation disorders (after stroke, cerebrovascular insufficiency, etc.); withdrawal syndrome in case of chronic alcoholism (in combination with specific therapy); hemophthalmus and retinal hemorrhages of various etiologies; thrombosis of the central retinal vein and its branches;

retinopathy of various etiologies (diabetic, hypertonic); low efficiency, mental and physical overstrain (incl. athletes).

Contraindications:
Hypersensitivity to the components of the drug, increased intracranial pressure (caused by violation of the venous outflow or intracranial tumors), age below 18 years (effectiveness and safety not guaranteed), pregnancy and lactation.

With Caution:
Liver and / or kidneys diseases.

Dosage and administration:
1. Cardiovascular diseases: with IHD (myocardial infarction) the drug is administered (as s part of complex therapy) intravenously 0.5-1.0 g a day (5-10 ml), applying the whole dose at once or dividing it into 2 injections.
With IHD (stable angina), chronic heart failure and dyshormonal cardiomyopathy the drug is administered (as s part of complex therapy) intravenously 0.5-1.0 g a day (5-10 ml), applying the whole dose at once or dividing it into 2 injections, or intramuscular 0.5 g 1-2 times a day. The course of treatment is 10-14 days. Afterwards it`s prescribed to take capsules orally according to the instruction. Duration of the whole course is 4-6 weeks.
2. Disorders of the cerebral circulation: during acute phase 5 ml intravenous once a day during 10 days. Afterwards it`s prescribed to take capsules orally 500 mg – 1 g per day. Duration of the whole course is 4-6 weeks.
With chronic cerebral circulatory insufficiency (dyscirculatory encephalopathy) the drug is administered 0.5 g (5 ml) intravenous or intramuscular once a day for 10 days. Afterwards it`s prescribed to take capsules orally 500 mg according to the instruction. Duration of the whole course is 4-6 weeks.
Repeated courses (usually 2-3 times a year) are possible after consultation with a doctor.
3. Mental and physical overstrain (including athletes): 5 ml once a day intravenous or intramuscular during 10-14 days. If necessary, the therapy can be repeated in 2-3 weeks.
4. Chronic alcohol use: 5 ml twice a day, intravenous or intramuscular. Duration of the treatment course is 7-10 days.
5. Ophthalmology: 0.5 ml (0.05 g) parabulbarly during 10 days.

Side effects:
Rarely: allergic reactions (redness and itching of the skin, skin rash, swelling), psychomotor agitation, dyspepsia, tachycardia and blood pressure changes.
Very rarely: eosinophilia and general weakness.

Overdose:
The cases of Mildronate overdose are not described. The drug toxicity is low and cannot cause side effects, dangerous to the health of patients.
Symptoms: reduced blood pressure, accompanied by headache, tachycardia, dizziness and general weakness.
Treatment: symptomatic.

Interaction with other drugs:
Meldonium can be used simultaneously with antianginal agents, anticoagulants, antiaggregants, antiarrhythmics, bronchodilators and diuretics.
Meldonium can enhance the action of antianginal agents, some hypotensive drugs and cardiac glycosides.
Simultaneous use of Mildronate together with nitroglycerin, nifedipine, alpha-blockers, hypotensive drugs and peripheral vasodilators can cause mild tachycardia and arterial hypotension, therefore combine them with caution.

Special instructions:
In view of the possible stimulating effect, it is recommended to apply Mildronate no later than 5 pm.

Years of experience in the treatment of acute myocardial infarction and unstable angina shows that Mildronate is not a first-line drug for treatment of acute coronary syndrome.
Patients with chronic liver and kidneys diseases should be careful with the long-term use of the drug.
If you need to use the drug longer than for a month, you should consult a doctor.
There is not enough data on the use of Mildronate for children younger than 18 years.

Pregnancy and lactation:
The safety of the drug during pregnancy is not established. Therefore, to avoid possible adverse effects on the fetus, do not use Mildronate during pregnancy.
It is not known whether meldonium is excreted in breast milk. If you need to use the drug during lactation breastfeeding should be discontinued.

Influence on the ability to drive vehicles and operate mechanisms: no data.

Terms of release from pharmacy: on prescription.

Storage conditions: store at temperatures no higher than 25°C, do not freeze. Keep out of reach of children.

Shelf life: 4 years. Do not use beyond the expiration date printed on the package.

Country of manufacture: Latvia