ARGIDON

Instructions
on medical use of the drug

Trade name of the drug: Argidon.
MHH: Meldonia dihydrate + Arginine hydrochloride.
Dosage form: Solution for injection.
Composition: *one ampoule (5 ml) contains:*

- meldonium dihydrate 0.5 g;
- arginine hydrochloride 1.0 g;
- excipient: water for injection.

ATX code:
CO1CX
B05XB01
Clinical and pharmacological group: Means for improving metabolic tissue processes.
Pharmacological properties:
Pharmacodynamics:
Meldonia dihydrate is a structural analogue of gamma- butyrobetaine, a substance that is found in every cell of the human body.
Meldonia dihydrate reduces carnitine levels and the transport of long-chain fatty acids across cell membranes, preventing the accumulation of activated forms of unoxidized fatty acids in cells. Improves metabolic processes. During ischemia, it activates glycolysis. As a result of a decrease in carnitine synthesis, the content of gamma-butyrobetaine, which has a vasodilating effect, increases.
In acute myocardial infarction, it slows down tissue necrosis and shortens the rehabilitation period. In heart failure, it improves myocardial contractility and increases exercise tolerance. The drug stimulates physical performance, relieves mental and physical stress. Activates cellular and humoral immunity.
Eliminates withdrawal syndrome in chronic alcoholism.
Arginine (a- amino -d- guanidinovaleric acid) is an amino acid that belongs to the class of conditionally essential amino acids and is an active and versatile cellular regulator of numerous vital functions of the body, exhibiting protective effects that are important in a critical condition of the body.
Arginine has antihypoxic, membrane stabilizing, cytoprotective, antioxidant, antiradical , detoxification effects, manifests itself as an active regulator of intermediate metabolism and energy supply processes, and plays a certain role in maintaining hormonal balance in the body. It is known that arginine increases the blood levels of insulin, glucagon, growth hormone and prolactin, takes part in the synthesis of proline, agmatine, is involved in the processes of fibrinogenolysis, spermatogenesis, and has a membrane depolarizing effect. Arginine is one of the main substrates in the urea synthesis cycle in the liver.
The hypoammonemic effect of the drug is realized by activating the conversion of ammonia to urea. It has a hepatoprotective effect due to antioxidant, antihypoxic and membrane-stabilizing activity, and has a positive effect on energy supply processes in hepatocytes .
Arginine is a substrate for NO synthase, an enzyme that catalyzes the synthesis of nitric oxide in endothelial cells. The drug increases the level of cyclic guanidine monophosphate (cGMP) in the vascular endothelium, reduces the activation and adhesion of leukocytes and platelets to the vascular endothelium, suppresses the synthesis of adhesion proteins VCAM-1 and

MCP-1, thus preventing the formation and development of atherosclerotic plaques, suppresses the synthesis of endothelin - 1, which is a powerful vasoconstrictor and stimulator of proliferation and migration of smooth myocytes of the vascular wall. Arginine also suppresses the synthesis of asymmetric dimethylarginine, a powerful endogenous stimulator of oxidative stress. The drug stimulates the activity of the thymus gland, which produces T cells, regulates blood glucose levels during exercise. It has an acid-producing effect and helps correct the acid-base balance.

Pharmacokinetics:

The bioavailability of the drug after intravenous administration is 100%. With $_{max}$ in plasma is achieved immediately after administration.

It is biotransformed in the body to form two main metabolites, which are excreted by the kidneys. The half-life ($T_{1/2}$) depends on the dose and is 3-6 hours.

Indications:

- ischemic heart disease, chronic heart failure;
- complex therapy of acute and chronic disorders of the blood supply to the brain (stroke and cerebrovascular insufficiency);
- vascular pathology and dystrophic diseases of the retina (hemophthalmos and hemorrhages, thrombosis of the central retinal vein and its branches, retinopathy , including diabetic and hypertensive);
- withdrawal syndrome in chronic alcoholism (in combination with specific therapy for alcoholism);
- stimulation of spermatogenesis in male infertility;
- decreased performance;
- heavy mental and physical stress, incl . in high performance sports (for athletes, it is necessary to take into account that the drug can give a positive result during doping control).

Directions for use and dosage:

The drug is administered intramuscularly and intravenously. When administered by drip, the drug is pre-diluted in 100-200 ml of 0.9% sodium chloride solution.

It is not recommended to mix with glucose or other drugs!

The initial rate of administration is 10 drops/min., after 20 minutes from the start the rate is increased to 30 drops/min. The daily dosage of the drug is 5-10 ml. The average course of therapy is 5-10 days.

Cardiovascular diseases (as part of complex therapy):

IHD (myocardial infarction) - intravenous bolus 0.5–1 g per day (5–10 ml of the drug);

IHD (stable angina); CHF and cardiomyopathy due to dyshormonal disorders - 0.5–1 g per day (5–10 ml of the drug) intravenously or 0.5 g (5 ml of the drug) intravenously 1–2 times a day, course treatment – 10–14 days.

Cerebrovascular accident: As part of complex therapy in the acute phase, 0.5 g (5 ml of the drug) 1 time per day IV for 10 days.

For chronic cerebral circulatory failure (dyscirculatory encephalopathy) - 0.5 g (5 ml of the drug IM or IV once a day for 10 days. Repeated courses (usually 2-3 times a year) are possible after consultation with doctor.

Ophthalmopathology (hemophthalmia and retinal hemorrhages of various etiologies, thrombosis of the central retinal vein and its branches, retinopathy *of various etiologies (diabetic, hypertensive)* 0.05 g (0.5 ml of the drug) parabulbarly for 10 days. Including used in as part of combination therapy.

Mental and physical overload: 0.5 g (5 ml of the drug) IM or IV 1 time per day. The course of treatment is 10–14 days. If necessary, treatment is repeated after 2–3 weeks .

Chronic alcoholism: 0.5 g (5 ml of the drug) IM or IV 2 times a day. The course of treatment is 7–10 days.

Side effects:
Intravenous administration of Argidon can cause a burning sensation and heat in the body, headache, local inflammation of the vein at the injection site, and in some cases allergic reactions may occur, usually in the form of urticaria.
In rare cases - itching, dyspeptic symptoms, tachycardia, agitation, changes in blood pressure.
Contraindications:
- hypersensitivity to the drug;
- severe liver and kidney failure;
- pregnancy and lactation;
- hyperchloremic acidosis;
- children under 18 years of age;
- increased intracranial pressure (due to impaired venous outflow, intracranial tumors).

Overdose:
Manifests itself in hypoglycemic conditions (sweating, weakness, anxiety, tremors of the limbs, tachycardia), allergic reactions and metabolic acidosis.
To relieve such conditions, the drug is stopped, desensitizing treatment is carried out with antihistamines and alkalizing drugs, saluretics and crystalloid solutions (0.9% saline solution, 5% glucose or dextrose solution) are used.
Pregnancy and lactation:
Argidon is not recommended for use during pregnancy and lactation.
Interaction with other drugs:
Argidon enhances the effect of antianginal drugs, some antihypertensive drugs and cardiac glycosides.
The drug is compatible with anticoagulants, antiplatelet agents, bronchodilators, antiarrhythmic, antianginal and diuretic drugs.
When used together with Argidon nitroglycerin, nifedipine, alpha- blockers, antihypertensive drugs and peripheral vasodilators may develop moderate tachycardia and arterial hypotension.
When taken together with aminophylline, an increase in insulin levels in the blood and hypoglycemia may occur. The use of Argidon after a course of treatment with spironolactone or other potassium-sparing diuretics causes persistent hyperkalemia - an increase in the amount of potassium in the blood. The drug enhances the effects of alcohol, psychostimulants and nicotine.
Special instructions:
With chronic liver and kidney diseases, long-term use of the drug should be done with caution.
Due to the possibility of developing an stimulating effect, the drug is recommended to be used in the first half of the day. There is insufficient data on the use of Argidon in children.
Release form:
Solution for injection: 0.5 g + 1.0 g/5 ml in ampoules, 10 ampoules in a carton.
Storage conditions:
In a place protected from light and out of reach of children at a temperature not higher than 25 °C. Do not freeze!
Best before date:
2 years. The drug should not be used after the expiration date indicated on the packaging.
Vacation conditions:
On prescription.

Made for:
MAXX PHARM LTD.
London, Great Britain