Mildronate® capsules

Registration number:
LS-001115-120511 (ЛС-001115-120511)

Trade name:
MILDRONATE®.

International Nonproprietary Name (INN):
Meldonium

Dosage form:
Capsules

Composition
1 capsule contains:
active substance: meldonium dihydrate – 250mg/500 mg;
excipients: potato starch - 27.2 mg, colloidal silicon dioxide - 10.8 mg, calcium stearate - 5.4 mg;
capsule (body and cap): titanium dioxide (E 171) - 2%, gelatin - 98%.

Description
Hard gelatin capsules № 00, body and cap white color. Contents - white crystalline powder with a faint odor. The powder is hygroscopic.

Pharmacotherapeutic group:
metabolic agent

ATX code: C01EV (C01EB)

Pharmacological properties

Pharmacodynamics
Meldonium is a synthetic analog of gamma-butyrobetaine, a substance that is found in every cell of the human body. It inhibits gamma-butyrobetaine hydroxinase, reduces carnitine synthesis and transport of long-chain fatty acids through cell membranes, prevents accumulation of activated forms of unoxidized fatty acids in cells - derivatives of acylcarnitine and acyl coenzyme A.
Cardioprotective agent that normalizes myocardial metabolism. In conditions of ischemia, meldonium restores equilibrium between the processes of oxygen delivery and its consumption in cells, prevents violation of adenosine triphosphate (ATP) transport; at the same time it activates glycolysis, which proceeds without additional oxygen consumption. As a result of a decrease in carnitine concentration, gamma-butyrobetaine, which has vasodilating properties, is synthesized intensively. The mechanism of action determines the diversity of its pharmacological effects: increased performance, reduction of symptoms of mental and physical overstrain, activation of tissue and humoral immunity, cardioprotective effect. In case of acute ischemic myocardial injury, meldonium slows down the formation of necrotic zone, shortens the rehabilitation period.
In heart failure increases myocardial contractility, increases tolerance to exercise, reduces the frequency of angina attacks. In acute and chronic ischemic cerebral circulatory disorders improves blood circulation in the focus of ischemia, promotes blood redistribution in favor of the ischemic area.
It is effective in case of vascular and dystrophic pathology of the vessels of the eye fundus. It is also characterized by tonic effect on the central nervous system, elimination of functional disorders of somatic and autonomic nervous systems in patients with chronic alcoholism in withdrawal syndrome.

Pharmacokinetics
After oral administration meldonium is rapidly absorbed, bioavailability - 78%. Time to reach maximum plasma concentration is 1 - 2 hours after ingestion. It is metabolized mainly in the liver with the formation of two major metabolites, which are excreted by the kidneys. The elimination half-life (T1/2) at ingestion depends on the dose and is 3-6 hours.

Indications for use
In the complex therapy of ischemic heart disease (angina pectoris, myocardial infarction), chronic heart failure and dyshormonal cardiomyopathy, as well as in the complex therapy of subacute and chronic disorders of blood supply to the brain (after stroke, cerebrovascular insufficiency).
Reduced performance; mental and physical overload (including athletes).

Withdrawal syndrome in chronic alcoholism (in combination with specific therapy).

Contraindications

Hypersensitivity to the active substance and other components of the drug,
increased intracranial pressure (with impaired venous outflow, intracranial tumors),
age under 18 years (efficacy and safety have not been established),
pregnancy, lactation.

With caution:

In liver and/or kidney disease.

How to use and dosage

Due to the possible development of excitatory effect, it is recommended to use in the morning and no later than 17.00 when taken several times a day.

Capsules 250 mg

The daily dosage for adults is 500 mg (2 caps.). You can take either the entire dose in the morning or divide it into 2 doses twice a day. The duration of the treatment course is 10–14 days. If necessary, repeat after 2-3 weeks.

Capsules 500 mg

1. Coronary heart disease (angina pectoris, myocardial infarction), chronic heart failure and dyshormonal cardiomyopathy

As part of complex therapy 500 mg - 1 g daily orally, applying the entire dose at once or dividing it into 2 times. Course of treatment - 4-6 weeks.
Dyshormonal cardiomyopathy - as part of a complex therapy of 500 mg orally per day. Course of treatment - 12 days.

2. Subacute and chronic disorders of blood supply to the brain (after stroke, cerebrovascular insufficiency)

As a part of complex therapy after the end of the course of injection therapy with Mildronate® , the drug continues to be taken orally at 500 mg - 1 g per day, applying the whole dose at once or dividing it into 2 times. The course of treatment - 4-6 weeks.
In chronic disorders - as a part of complex therapy - 500 mg orally per day. Total course of treatment - 4-6 weeks.
Repeated courses (usually 2-3 times a year) is possible after consultation with a doctor.

3. Reduced working capacity; mental and physical overload (including athletes)

Adults - orally 500 mg 2 times a day. Course of treatment - 10-14 days. If necessary, treatment is repeated in 2-3 weeks.
Athletes 500 mg - 1 g orally 2 times a day before training. Duration of the course in the preparatory training period - 14 - 21 days, in the period of competition - 10 -14 days.

4. Withdrawal syndrome in chronic alcoholism (in combination with specific therapy)

Intravenously 500 mg 4 times a day. Course of treatment - 7 - 10 days.

Side effects

Rarely - allergic reactions (redness and itching of the skin, skin rash, urticaria, angioedema), as well as - dyspeptic phenomena, tachycardia, decreased or increased blood pressure, hyperexcitability. Very rare - eosinophilia, general weakness.

Overdose

Symptoms: decrease in blood pressure accompanied by headache, tachycardia, dizziness and general *weakness.*
Treatment: symptomatic.

Interaction with other medicinal preparations

It enhances the effect of coronary dilators, some hypotensive agents, cardiac glycosides. It can be combined with prolonged forms of nitrates, other antianginal agents, anticoagulants, antiaggregants, antiarrhythmic agents, diuretics, bronchodilators.
Due to possible development of tachycardia and arterial hypotension, caution should be exercised in combination with nitroglycerin (for

sublingual use) and hypotensive agents (especially alpha-adrenoblockers and short-acting forms of nifedipine).

Special instructions

Patients with chronic liver and kidney diseases should be cautious during prolonged use of the drug.
There are no sufficient data on the use of Mildronate® in children under 18 years of age.

Pregnancy and lactation period

Safety of the drug use during pregnancy has not been established. To avoid possible adverse effects on the fetus, use of Mildronate® during pregnancy is not recommended.
It is unknown whether meldonium is excreted into breast milk. If treatment with the preparation Mildronate® for the mother is necessary, breastfeeding of the child is discontinued.

Effect on the ability to drive vehicles and mechanisms

There are no data on the adverse effect of the preparation Mildronate® on the ability to drive vehicles and mechanisms.

Form of release

Capsules 500 mg. 10 capsules each in a contoured cell package made of polyvinylchloride film with polyvinylidene chloride coating and aluminum foil.
2 or 6 contoured cell packs together with instructions for use are placed in a cardboard pack.

Storage conditions

Store in a dry place at a temperature not exceeding 25 °C.
Keep out of reach of children.

Shelf life

4 years.
Do not use after the expiration date indicated on the package.

Conditions of release from pharmacies

By prescription.

Manufacturer

JSC "Grindeks". 53 Krustpils Street, Riga, LV-1057, Latvia