APPROVED
The Order of Ministry of Health of Ukraine
29.07.2022 № 1352
Registration certificate
№ UA/16294/01/01

INSTRUCTION
for medical use

DIACOBAL®

Composition:
active substance: methylcobalamin;
1 tablet contains methylcobalamin 500 mcg;
excipients: microcrystalline cellulose, pregelatinized starch, povidone K 30, anhydrous colloidal silicon dioxide, talcum powder, stearic acid, ethyl cellulose, titanium dioxide (E 171), polyethylene glycol 400, coating Opadry 03F565012 brown: hypromellose, titanium dioxide (E 171), iron oxide red (E 172), polyethylene glycol, talcum powder.

Pharmaceutical form. Film-coated tablets.
Main physical and chemical properties: round, biconvex, film-coated tablets of brown color.

Pharmacotherapeutic group.
Vitamin B_{12} preparations (cyanocobalamin and its analogues). ATC code B03B A05.

Pharmacological properties.
Pharmacodynamics.
Methylcobalamin is one of the active forms of vitamin B_{12}. Vitamin B_{12} is required for the synthesis of nuclear protein and myelin, cell reproduction, normal growth, and normal erythropoiesis. In comparison with other forms of vitamin B_{12}, methylcobalamin at the subcellular level is better transported to organelles of neurons and promotes protein and nucleic acid synthesis. It is exactly due to this property that it is more effective in the treatment of diseases of the nervous system.
Methylcobalamin plays an important role in transmethylation processes as a coenzyme of methionine synthase, an enzyme involved in the conversion of homocysteine to methionine in the reactions of methylation of proteins and DNA. Methylcobalamin is known to normalize the axonal transport of protein complexes and promote the regeneration of axons. Methylcobalamin also promotes myelination of neurons by stimulating the synthesis of phospholipids (in particular, lecithin – the main lipid component of the myelin sheath of nerve endings). In addition, methylcobalamin restores delayed synaptic transmission and reduces the content of neurotransmitters to normal levels.
The use of therapeutic doses of methylcobalamin promotes detoxification processes in the nervous system due to the growth of the content of tetrahydrofolate. Methylcobalamin is also a coenzyme in the reaction of conversion of homocysteine to S-adenosyl methionine, which is a universal donor of methyl groups, which causes the activation of trans-methylation reactions.
Pharmacokinetics.
Upon single oral administration of the drug in the fasting state in single doses of 120 mcg and 1500 mcg in healthy adult male volunteers the peak plasma concentration of total vitamin B_{12} is reached after 3 hours for both doses, this indicating parameter is dose-dependent. From 40% to

90% of the aggregate amount of total B_{12} excreted in the urine within 24 hours following the administration, was excreted within the first 8 hours. The is no evidence for a single dose of 1500 mcg.
For further multiple oral administration at a dose of 1500 mcg per day for 12 consecutive weeks in healthy adult male volunteers, peak serum concentrations of total vitamin B_{12} were being determined up to 4 weeks after the last dose. The serum concentration increases during the first 4 weeks after the start of administration, reaching a level that exceeds the baseline by approximately twice. Thereafter, a gradual increase was observed, reaching a maximum of 2.8 times the initial value, in the 12th week of taking the drug. Serum concentration decreases after the last dose (12 weeks), but still exceeds the baseline value 1.8 times after 4 weeks following the last dose of the drug.

Clinical characteristics.
Indications.
Peripheral neuropathy.

Contraindications.
Known hypersensitivity to methylcobalamin or other components of the drug.
Erythremia, erythrocytosis.
Neoplasms, except for cases accompanied by megaloblastic anemia and vitamin B_{12} deficiency.
Acute thromboembolic diseases.
Angina of effort of high functional class.

Interaction with other medicinal products and other types of interaction.
Co-administration with folic acid improves absorption and uptaking of methylcobalamin.
Other drugs containing vitamin B_{12} should not be co-prescribed.
Chloramphenicol reduces the hematopoietic response of reticulocytes to the drug. If such a combination cannot be avoided, the blood parameters should be closely monitored.
Medicinal products that can reduce the absorption of vitamin B_{12}: aminosalicylic acid, antibiotics, colchicine, cholestiramine, histamine receptor H_2 blockers, metformin, neomycin, nitrous oxide, phenytoin, phenobarbital, primidone, proton pump inhibitors, zidovudine.
When co-administered with thiamine, the risk of allergic reactions caused by thiamine increases.
Oral contraceptives reduce the blood concentration of vitamin B_{12} in the blood.

Administration details.
The drug Diacobal should be used with caution in patients with history of signs of allergy, hepatic disorders.
Prolonged use of high doses of the drug is not recommended for patients whose occupational activity is related to mercury or mercury-containing compounds.
The use of vitamin B_{12} with drugs that increase blood clotting is not recommended. During treatment with the drug, peripheral blood parameters need to be monitored. Care should be exercised and blood clotting should be monitored during treatment of patients with underlying risk of thrombosis and patients with angina. The dose of the drug should be reduced or the treatment should be temporarily suspended in case of tendency for the development of leuko- and erythrocytosis.

Use during pregnancy or breastfeeding.
There is no data about the safety of using the drug during pregnancy or breastfeeding.

Effect on reaction rate when driving motor transport or using other mechanisms.
There is no data regarding the negative effects of the drug on the speed of psychomotor reactions.

Dosage and administration.
The drug is for oral use by adults.
The recommended daily dose is 1500 mcg (3 tablets) which is divided into three doses.
The duration of therapy depends on the nature and course of the disease and is determined individually. The drug should be discontinued in the absence of a clinical effect after continuous administration of the drug for 1 month.

Children.
The use of the drug is contraindicated in children (under the age of 18).

Overdose.
Symptoms: nausea, vomiting, dizziness, agitation, tachycardia.
Treatment: symptomatic and supportive treatment.

Adverse reactions.
Gastrointestinal tract: anorexia, nausea, vomiting, diarrhea.
Central nervous system: anxiety, headache, dizziness, migraine, severe anxiety disorders, agitation, insomnia.
Cardiovascular system: palpitations, tachycardia, heart pain.
Immune system: hypersensitivity reactions, including urticaria, anaphylactic shock, anaphylactoid reactions.
Musculoskeletal system: muscle pain, join pain.
Skin: hyperemia, pruritus, rash, acne.
Blood and lymphatic system: thrombosis, hypercoagulation.
General disorders: increased sweating, general weakness, fever.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is an important procedure. It allows continued monitoring of the benefit/risk balance of this medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system and to the applicant via the feedback form at the website: https://kusum.ua/pharmacovigilance/.

Shelf life.
2 years.

Storage conditions.
Store at a temperature not more than 25 ºC.
Keep out of reach of children.

Package.
10 tablets are in a blister; 3 or 10 blisters are in a carton package.

Conditions of supply.
By prescription.

Manufacturer.
LLC “KUSUM PHARM”.

Address of manufacturer and manufacturing site.
40020, Ukraine, Sumy region, Sumy, Skryabina Str., 54.

Last revision date.
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