APPROVED
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22.02.2021 No. 301
Registration certificate
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INSTRUCTION
for medical use

NEUROCOBAL®

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

Pharmaceutical form. Film-coated tablets.
Basic physical and chemical properties: round biconvex brown film-coated tablets.

Pharmacotherapeutic group.
Vitamin B_{12} (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 necessary 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 stimulates the synthesis of proteins and nucleic acids. It is thanks to this property that it is more effective in the treatment of nervous system diseases.
Methylcobalamin plays an important role in the processes of transmethylation as a coenzyme of methionine synthetase, an enzyme involved in the conversion of homocysteine to methionine in protein and DNA methylation reactions. It is known that methylcobalamin normalizes the axonal transport of protein complexes and promotes axons regeneration. Also, methylcobalamin promotes myelination of neurons due to stimulation of phospholipid synthesis (in particular, lecithin – the main lipid component of the myelin sheath of nerve endings). In addition, methylcobalamin restores delayed synaptic transmission and reduces the number of neurotransmitters to normal levels.
The use of therapeutic doses of methylcobalamin promotes detoxification processes in the nervous system due to an increase in the concentration of tetrahydrofolate. Also, methylcobalamin is a coenzyme in the reaction of the conversion of homocysteine into S-adenosylmethionine, which is a universal donor of methyl groups, that leads to activation of transmethylation reactions.
Pharmacokinetics.

With a single oral administration of the drug on an empty stomach in single doses of 120 mcg and 1500 mcg in healthy adult male volunteers, the peak concentration of total vitamin B_{12} in blood plasma is reached after 3 hours for both doses, this indicator is dose-dependent. 40–90% of total B_{12} excreted in the urine 24 hours after administration, are excreted within the first 8 hours. There is no confirmation for a single dose of 1500 mcg.
With further repeated oral administration at a dose of 1500 μg/day for 12 consecutive weeks, peak concentrations of total vitamin B_{12} were determined in healthy adult male volunteers in blood plasma 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 initial value by about 2 times. After this, gradual increase is observed, which reaches a maximum of 2.8 times the initial value at the 12th week of taking the drug. Serum concentration decreases after the last dose (12 weeks), but still exceeds the initial value by 1.8 times 4 weeks after the last dose.

Clinical characteristics.
Indications.
Peripheral neuropathy.

Contraindications.
Hypersensitivity to methylcobalamin or other components of the drug.
Erythremia, erythrocytosis.
Neoplasms, except in cases accompanied by megaloblastic anemia and vitamin B_{12} deficiency.
Acute thromboembolic diseases.
Exertional stenocardia of high functional class.

Interaction with other medicinal products and other forms of interaction.
Simultaneous administration with folic acid improves the absorption and uptake of methylcobalamin.
Do not prescribe with other drugs containing vitamin B_{12}.
Chloramphenicol reduces the hematopoietic response of reticulocytes to the drug. If you cannot avoid such a combination, you need to carefully monitor blood counts.
Medicines that can reduce the absorption of vitamin B_{12}: aminosalicylic acid, antibiotics, colchicine, cholestyramine, H_2 receptor blockers, metformin, neomycin, nitrous oxide, phenytoin, phenobarbital, primidone, proton pump inhibitors, zidovudine.
With simultaneous use with thiamine, the risk of allergic reactions caused by thiamine increases.
Oral contraceptives reduce the concentration of vitamin B_{12} in the blood.

Special warnings and precautions for use.
The drug should be used with caution in patients with manifestations of allergies, a history of liver disease.
Long-term use of high doses of the drug is not recommended for patients whose professional activity is associated with mercury or compounds containing mercury.
Vitamin B_{12} is not recommended with drugs that increase blood coagulability. During the treatment period, it is necessary to monitor peripheral blood counts. Concerning patients with a tendency to thrombosis and patients with angina pectoris, it is necessary to use caution and control blood coagulation during treatment.
With a tendency to develop leuko- and erythrocytosis, the dose of the drug must be reduced or temporarily suspended.

Pregnancy or lactation.
There is no data on the use of the drug during pregnancy and lactation.

Ability to influence reaction rate while driving cars or operating other mechanisms.
There is no data on the negative effect of the drug on the rate of psychomotor reactions.

Posology and method of administration.
The drug is administered orally to adults.
The recommended daily dose is 1500 μg (3 tablets), which is divided into three doses.
The duration of the treatment course depends on the nature and course of the disease and is determined individually. If there is no clinical effect after continuous intake of the drug within 1 month, the drug should be discontinued.

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

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

Side effects.
Gastrointestinal tract disorders: anorexia, nausea, vomiting, diarrhea.
Central nervous system disorders: anxiety, headache, dizziness, migraine, severe anxiety disorders, agitation, insomnia.
Cardiovascular system disorders: accelerated heartbeat, tachycardia, heart pain.
Immune system disorders: hypersensitivity reactions, including urticaria, anaphylactic shock, anaphylactoid reactions.
Musculoskeletal system disorders: muscle pain, joint pain.
Skin disorders: hyperemia, itching, rash, acne.
Blood system and lymphatic system disorders: thrombosis, hypercoagulation.
General disorders: increased sweating, generalized weakness, fever.

Shelf-life.
3 years.

Storage conditions.
Store at the temperature below 25ºC.
Keep out of reach of children.

Package.
10 tablets in a blister, 3 or 10 blisters in a carton pack.
30 tablets in a blister, 3 blisters in a carton pack.

Conditions of supply.
By prescription.

Manufacturer.
KUSUM HEALTHCARE PVT LTD.

Location of manufacturer and its address of its business activity.
SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.
Date of last revision.