

**PACKAGE LEAFLET**  
**for medical use of a medicinal product**

**CYANOCOBALAMIN-DARNITSA**  
**VITAMIN B<sub>12</sub>-DARNITSA**

***Qualitative and quantitative composition:***

*active substance:* cyanocobalamin;

1 ml of solution contains cyanocobalamin 0.5 mg;

*List of excipients:* sodium chloride, sodium acetate trihydrate, acetic acid, water for injection.

**Pharmaceutical form.** Solution for injection.

*Main physical and chemical properties:* clear red liquid.

**Pharmacotherapeutic group.**

Vitamin B<sub>12</sub> (cyanocobalamin and its analogues). Cyanocobalamin. ATC code B03B A01.

***Pharmacological properties.***

*Pharmacodynamic properties.*

Vitamin B<sub>12</sub> (cyanocobalamin) has a metabolic, hematopoietic effects. In the body (mainly in the liver) is converted into a coenzyme form - adenosylcobalamin, or cobamamide, which is the active form of vitamin B<sub>12</sub>. Cobamamide is part of numerous enzymes, including reductase, which reduces folic acid to tetrahydrofolic. It has high biological activity. Cobamamide is involved in the transfer of methyl and other monocarbon fragments, therefore it is necessary for the formation of deoxyribose and DNA, creatine, methionine - a donor of methyl groups, in the synthesis of lipotropic factor - choline, for the conversion of methylmalonic acid into succinic acid, which is part of myelin, for the utilization of propionic acid. Cobamamide is essential for normal hematopoiesis because it promotes the maturation of red blood cells. It takes part in the synthesis and accumulation of compounds containing sulfhydryl groups in erythrocytes, which increases their tolerance to hemolysis. It activates the blood coagulation system, in high doses causes an increase in thromboplastic activity and prothrombin activity. It reduces blood cholesterol levels. It positively effects on the function of the liver and nervous system. It increases the tissue's ability to regenerate.

*Pharmacokinetic properties.*

When administered parenterally, vitamin B<sub>12</sub> enters the systemic circulation rapidly. In the blood, it binds to transcobalamin I and II, which transports it to the tissues. It is deposited mainly in the liver. The plasma protein binding is 90 %. The time to reach maximum concentration (T<sub>Cmax</sub>) after subcutaneous or intramuscular administration is about 1 hour. It is excreted from the liver with bile into the intestines and reabsorbed into the blood. The half-life (T<sub>1/2</sub>) from the liver is 500 days. It is excreted with normal renal function - 7-10% by the kidneys, about 50% - with fecal masses; with reduced renal function - 0-7% by the kidneys, 70-100% - with fecal masses. It penetrates the placental barrier.

**Clinical particulars.**

***Therapeutic indications.***

Treatment of malignant, post-hemorrhagic and iron deficiency anemias, aplastic anemias in children, alimentary anemias caused by toxic substances and medicinal products associated with vitamin B<sub>12</sub> deficiency, regardless of the cause of the deficiency (gastrectomy, helminthic infestations, impaired intestinal absorption, pregnancy). Polyneuritis, trigeminal neuralgia, radiculitis, causalgia, migraine, diabetic neuritis, amyotrophic lateral sclerosis, cerebral palsy, Down's disease, alcoholic delirium. Use in children with dystrophy, after infectious diseases, with sprue (together with folic acid), for

liver diseases (hepatitis, cirrhosis, Botkin's disease), radiation sickness, psoriasis, herpetic dermatitis, neurodermatitis, photodermatitis.

### ***Contraindications.***

Hypersensitivity to components of the medicinal product. Erythremia, erythrocytosis. Neoplasms, except in cases accompanied by megaloblastic anemia and vitamin B<sub>12</sub> deficiency. Acute thromboembolic diseases. High functional class exertional angina.

### ***Interaction with other medicinal products and other forms of interaction.***

*Aminoglycosides, salicylates, antiepileptic drugs, colchicine, potassium medicinal products reduce the absorption of the medicinal product, affect its kinetics.*

*Concomitant use with kanamycin, neomycin, polymyxins, tetracyclines absorption of cyanocobalamin decreases.*

It is pharmaceutically incompatible with *ascorbic acid, heavy metal salts* (cyanocobalamin inactivation); *thiamine bromide, pyridoxine, riboflavin* (the cobalt ion contained in the cyanocobalamin molecule, destroys other vitamins).

*Thiamine - increases the risk of developing allergic reactions caused by thiamine.*

*Chloramphenicol - reduces the hematopoietic response to the medicinal product.*

*Oral contraceptives - reduce the concentration of cyanocobalamin in the blood.*

### ***Special warnings and precautions for use.***

Peripheral blood parameters should be monitored during therapy: on the 5-8th day from the beginning of treatment to determine the content of reticulocytes, the concentration of iron. The number of erythrocytes and hemoglobin, as well as the color index should be monitored for 1 month 1-2 times a week, and then - 2-4 times a month. Remission is achieved by increasing the number of erythrocytes to  $4.0-4.5 \times 10^{12}/l$ , when reaching normal erythrocyte size, disappearance of aniso- and poikilocytosis, normalization of reticulocyte content after reticulocyte crisis. After achieving hematological remission, peripheral blood control should be performed at least once every 4-6 months.

With a tendency to develop leuko- and erythrocytosis, the dose of the medicinal product should be reduced or temporarily suspended.

Cyanocobalamin cannot be used with medicinal products that increase blood clotting.

In the course of treatment, it is necessary to be careful and control blood clotting in persons with a tendency to thrombus formation and patients with angina pectoris.

### ***Important information about excipients.***

This medicinal product contains less than 1 mmol (23 mg)/dose of sodium, i.e. essentially 'sodium-free'.

### ***Fertility, pregnancy and lactation.***

Use with caution under medical supervision during pregnancy (there are some data on the teratogenic effects of vitamin B<sub>12</sub> in high doses) or breastfeeding, taking into account the benefit/risk analysis.

### ***Effects on ability to drive and use machines.***

During treatment, it is necessary to refrain from driving and potentially dangerous activities that require increased attention and speed of psychomotor reactions.

### ***Posology and method of administration.***

The medicinal product is administered subcutaneously, intramuscularly, intravenously, and in case of lateral funicular myelosis and amyotrophic sclerosis, also intralumbar.

#### **Adults**

In case of B<sub>12</sub>-deficient anemias, the medicinal product should be used in doses of 100-200 µg (0.1-0.2 mg) every other day until remission is achieved.

When symptoms of funicular myelosis appear and macrocytic anemia with damage to the nervous system, cyanocobalamin should be used in a single dose of 400-500 µg (0.4-0.5 mg) or more. During the first week, enter daily, and then at intervals of 5-7 days (at the same time prescribe folic acid). In severe cases, inject into the spinal canal, starting with a single dose of 15-30 µg, with each subsequent injection, increase the dose (50, 100, 150, 200 µg). Intralumbar injections should be given every 3 days, for a total of 8-10 injections per course. In the period of remission in the absence of the phenomena of funicular myelosis for maintenance therapy, prescribe 100 µg twice a month, in the presence of neurological symptoms - 200-400 µg 2-4 times a month.

*For amyotrophic lateral sclerosis, encephalomyelitis, neurological diseases with pain*, the medicinal product should be administered in increasing doses from 200 to 500 µg per injection (in case of improvement - 100 µg per day). The course of treatment is 14 days.

For injuries of peripheral nerves, prescribe 200-400 µg 1 time in 2 days within 40-45 days.

For hepatitis and cirrhosis of the liver, prescribe 15-30 µg per day or 100 µg every other day for 25-40 days.

For diabetic neuropathy, sprue, radiation sickness, administer 60-100 µg daily for 20-30 days.

In case of vitamin B<sub>12</sub> deficiency for treatment - intramuscularly and intravenously 1 mg every day for 1-2 weeks, maintenance dose - 1-2 mg intramuscularly or intravenously from 1 time per week to 1 time per month. The duration of cyanocobalamin treatment and repeat courses depend on the course of the disease and the effectiveness of treatment.

### Children

Inject only subcutaneously.

*For posthemorrhagic and iron deficiency anemia*, prescribe 30-100 µg 2-3 times a week.

*For aplastic anemia* in children, administer 100 µg before the onset of clinical and hematological improvement.

*For anemias of an alimentary nature* in childhood, prescribe 30 µg for 15 days.

*For dystrophies in young children, Down's disease and infantile cerebral paralysis*, prescribe 15-30 µg every other day.

*For hepatitis and cirrhosis of the liver*, children should be prescribed 15-30 µg per day or 100 µg every other day for 25-40 days.

### *Children.*

The dosage form at a dosage of 0.5 mg/ml should not be used in children under 3 years of age.

Inject only subcutaneously.

### ***Overdose.***

*Symptoms:* pulmonary edema, congestive heart failure, peripheral vascular thrombosis.

*Treatment:* symptomatic.

### ***Undesirable effects.***

*Gastrointestinal disorders:* liquefaction of feces.

*Metabolism and nutrition disorders:* acne, bullous rashes, nausea, sweating, impaired purine metabolism, hypokalemia.

*Nervous system disorders:* headache, dizziness, nervous excitement, drowsiness, muscle paralysis, loss of consciousness.

*Cardiac disorders:* tachycardia, pain in the region of the heart, congestive heart failure, peripheral vascular thrombosis, low blood pressure, cardiac arrest.

*Blood system disorders:* hypercoagulation.

*Immune system disorders:* allergic reactions, including skin manifestations, including hyperemia, urticaria, rashes, itching, dermatitis, edema, including Quincke's edema; respiratory disorders, including asthma attack, anaphylactic shock, anaphylactoid reactions.

*General disorders and administration site conditions:* malaise, fever; at the injection site: hyperemia, itching, pain, edema, tightness of the skin and necrosis.

### *Reported suspected adverse reactions.*

Reporting suspected adverse reactions after registration of the medicinal product is an important procedure. This allows for continued monitoring of the benefit/risk ratio for the respective drug. Healthcare providers should be informed of any suspected adverse reactions through the national alert system.

***Shelf life.*** 2 years.

**Special precautions for storage.**

Store in the original package at a temperature below 25°C. Do not freeze.

Keep out of the reach of children.

***Incompatibilities.***

When used in one solution of cyanocobalamin with ascorbic acid, pyridoxine is the mutual destruction of vitamins occurs, with nicotinic acid - the destruction of cyanocobalamin, with riboflavin - the accumulation of cobalt ions.

**Nature and contents of container.**

1 ml per ampoule; 10 ampoules in a blister container; 1 blister containers in a pack.

**Category of release.** Prescription only medicine.

**Manufacturer** PrJSC “Pharmaceutical firm “Darnitsa”.

**The manufacturer's location and address of the place of business.**

13, Boryspilska street, Kyiv, 02093, Ukraine.

**Date of last revision.**

06.03.2020.