



Instruction for Use

Pharmacological Committee Ministries of Health of Georgia
Registration number № R- 014514, № R-015768.
Patent № P 2021 7254 B

GA-40 is a complex of peptides, obtained from the ecologically pure plant material. GA-40 contains a biochemically purified standardized combination of plant-origin natural peptides.

Composition

Acting substance: 0.2 mg of GA-40.

Supplement substances: 9.0 mg sodium chloride,
2,75 mg potassium dihydrophosphate, pH 7,4

Form of Production

GA-40 is produced in the form of injection solution ampule. The packing box contains 10 ampoules. Each vial contains 1 mg lyophilized powder of GA-40.

Pharmacological Group and Classification Code

Immunomodulator – code: LO3A; antineoplastic - code: L01C.

Pharmacological Properties

Preclinical and clinical trials show that the drug GA-40 is an immunomodulator and belongs to immunocorrectors of immunorehabilitation type. The drug GA-40 is characterized by direct anti-tumor and indirectly mediated by immunity anti-tumor action.

GA-40 possesses selective action. Unlike chemical preparations, GA-40 does not damage normal cells that define its safety action on any tissues and organs of the organism. GA-40 interacts with membrane DR receptors of death on the surface of the tumor cells and kills them by promoting apoptosis (programmed cellular death). GA-40 causes normalization of p53, p21 functions, and blocking of the glutathione system of a tumor.

GA-40 causes activation of anti-tumor systems of immunity. GA-40 interacts with the specific membrane receptors located on the surface of mononuclear cells of immunity (monocytes, macrophages). As a result, changes appear in the structure of phosphatidylserine and activation of Ca²⁺ +- of independent protein kinase C from a class of new or atypical and tyrosine protein kinases - Ca (PKCε), Ca²⁺ +-dependent on protein kinases +Ca (PKCα,) and the tyrosine protein kinases. Protein kinases way leads (TPK) to activation of a transcription factor of NF-kB and its translocation in a nucleus. Activation of NF-kB is expressed in the increase of production of a factor of necrosis of a tumor (TNF-α), interferon - γ (INF-γ), activating the expression of specific genes. The mechanism of action of GA-40 is the cornerstone of the processes of activation of cells of immunity possessing the ability to destroy cancer cells: natural killer cells (NK-cell), T-cytotoxic cells, macrophages, and neutrophils.

The anti-tumoral action of GA-40 is also caused by its anti-angiogenesis property. GA-40 inhibits the release of vascular epithelial cell growth factor (VEGF) by cancer cells. GA-40 inhibits the development of new blood vessels or the process of neovascularization in malignant neoplasm and metastases and practically prevents the spread of metastases in the body via the blood circulatory system. GA-40 shows the expressed antioxidant and cytoprotective activity (neutralization of free radicals) that is especially important for the treatment of cancer patients by traditional methods and in the period of preventive treatment. An increase in liver GA-40 causes the decrease in serotonin, lactic and pyruvate acids, xanthine, uric acid, hydrogen peroxide, and oxygen with two unpaired electrons and hydrogen with one unpaired electron. The latter ones are free radicals, a high amount of which can be observed in the bodies of patients with malignant tumors, especially after radiotherapy and chemotherapy.

GA-40 has immunocorrective properties that make a correction of the immune status of the organism and restore the quantitative and functional indicators T and B of immune cellular systems i.e. T-helper cells, T-cytotoxic cells, T-killers (NK-cells), macrophages, and granulocytes. It regulates the correlation of T-helper and T-suppressor cells. It also regulates the indicators of immunoglobulin's, stimulates the production of cytokines, including the tumor necrosis factor (TNF-a) and interferon's (INF).

GA-40 restores the functional activity of stem hemopoietic cells too, normalizing the content of leukocytes, erythrocytes, neutrophils, thrombocytes, lymphocytes, and other blood-forming elements.

GA-40 provides for normalization of the blood biochemical indicators – total protein, albumin, globulin, urea nitrogen, creatinine, bilirubin, glucose, as well as certain enzymes such as alanine-aminotransferase (ALT), aspartate-aminotransferase (AST), γ-glutamine-transpeptidase (γ-GP), and alkaline phosphatase. The preparation renders a positive influence on the dynamic contents in the bloodstream of carcinoembryonic antigens (CEA), alpha-fetoprotein (AFP), prostate-specific antigen (PSA), as well as the blood contents in mineral compounds of sodium, calcium, potassium, and others.

Indications GA-40 is applied to:

*** Malignant tumors**

- Monotherapy treatment with GA-40 is recommended at the early stages of tumor development. Permanent treatment of cancer patients with GA-40 is recommended, when the size of the tumor formation does not exceed 1 cm, it induces complete regression of the tumor and a full recovery of the patient.
- Monotherapy treatment with GA-40 is recommended in patients suffering from cancer, who have exhausted all methods of standard treatment. Permanent and long-term treatment with GA-40 reduces pain, improves a general condition, increases energy and vitality, improves the degree of life, and significantly increases life span.
- The use of GA-40 is recommended in combination with radiation and chemotherapy (before the therapy, in parallel with it and in the following period) for the achievement of high efficacy of treatment. The use of GA-40 in combination with radiation and chemotherapy increases the efficiency of treatment at its direct and anticancer action due to the immunity on tumor cells. Because detoxifying, antioxidant, and genoprotective properties of GA-40 significantly reduces the toxic effects of chemotherapy and radiation on the organism and protects it from the development of the formation of new tumors.
- The use of GA-40 is recommended before and after surgical intervention for the achievement of high efficiency of treatment. The treatment with GA-40 before the surgery provides the normalization of the indices of the immune system, suspension of neovascularization processes, blocking the distribution of metastases, destroying of existing and hidden metastases, and as a result, the localization of the primary foci of malignant tumor in the organism occurs and it is protected from the further development of postoperative recurrences.
- The use of GA-40 during leukemia is recommended in combination with radiation and chemotherapy. During acute and chronic myelogenous leukemia at the treatment with GA-40, the transformation of cancer cells into normal ones is observed and the improvement of formation of blood cells – hematopoietic processes, the toxic impact of chemotherapy on the organism reduces.

It may also be used:

- For leucosis - acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) monotherapy or as adjuvant therapy.
- For the treatment of benign tumors (fibroid, myoma, adenoma, cystose, etc.).
- During infection-inflammatory processes (pneumonia lobularis, bronchopneumonia, pulmonary tuberculosis, liver disorders (cirrhosis, hepatitis-C), chronic banal prostatitis, etc.)
- Nontoxic preventive treatment for patients at risk (genetic predisposition coupled with environmental challenges), and those with precancerous lesions.
- For prophylaxis. It is recommended for persons above 40-50 age to carry out a course of treatment twice a year, to allow us to get rid of senile non-specific diseases, to reduce the risk of oncological diseases, and to create a state of the organism in which susceptibility to virus and other infectious diseases is reduced to a minimum.

Dosage and Method of Application

GA-40 is used in the form of subcutaneous or intramuscular injections. Injections are carried out with a 1 ml insulin syringe (for no more than 100 kg of body weight) or a 2 ml syringe (for over 100 kg of body weight). The dose of one injection is 0.2 mg of GA-40 for every 100 kg of body weight.

- 1-100 kg body weight / 1.0 ml;
- 100-200 kg body weight / 2.0 ml;
- 200-300 kg body weight / 3.0 ml;

GA-40 is injected subcutaneously or intramuscularly, it is desirable into the buttock muscle with insulin syringe per 100 kg of body weight and below, and with 2 g syringe per 100 kg and above.

The injection is recommended to perform once a day after 6 pm. In severe cases, for intensive treatment course, the injection is recommended to perform twice a day - in the morning and evening with 12 hours intervals. The duration of one course of treatment makes up 30 days. The interval between courses is 10-14 days.

The treatment is continued until the complete regression of tumor or other diseases. In all the cases the course consists of at least 7 courses.

In severe forms of the disease, the intervals between the courses are not recommended.

For Prevention or Prophylaxis non-Toxic Treatment, the course of treatment (once a day) is repeated at intervals of 4-6 months

Immunotherapeutic drug GA-40, which has the ability for immune restoration, is used for prevention and prophylaxis in all above-mentioned cases, when the reason for the development of disease is a decreased (immunodeficiency) or overly aggressive immunity of the organism (at autoimmune disease).

Especially it deals with the prevention and prophylactic treatment of such widely distributed severe diseases, as:

- **Benign and malignant tumors.** At genetic predisposition to tumor diseases, which is closely connected to unfavorable factors of the environment. Despite the age, in the organism of healthy human, thousands of cancer cells are arise every day. Anti-tumor rings of a strong immune system recognize these cancer cells, cause their killing and protect the organism from the development of tumors. The risk of developing a tumor is high in the organism with a destroyed or weakened immune system.
- For the prevention of tumor development and its prophylactic treatment, a genoprotective properties of GA-40 are very significant. The activation of antitumor immunity with GA-40, antioxidant activity, the ability of detoxification protects the organism from internal and external negative factors, as well as from mutations due to chemo- and radiotherapy. GA-40 controls the expression of oncogenes and reduces the level of oncoproteins content, which weakens the risk of tumor development.
- **Viral infections** – at viral infections it is used for immunity enhancing, as the persons having a strong immunity without symptoms and any complications suffer such severe diseases as C hepatitis (HCV), cytomegalovirus (CMV), herpes virus (HSV-2), herpes zoster virus (VZV), meningitis virus, influenza virus, coronavirus, etc. The mechanism of antiviral action of GA-40 is associated with inhibition of virus penetration into the cell, enhancing antiviral immunity, as well as with the activation of B-lymphocytes, T-cytotoxic cells, NK-cells and macrophages, which provides the killing and neutralization of virus-infected cells, stimulates the synthesis of interferon, which blocks the replication of the virus.

Side Effects

In therapeutic dosage is non-toxic, with no side effects, it is possible to reveal hypersensitivity towards the components.

Contraindications

It is not revealed.

Pregnancy and Breastfeeding

Ga-40 is used during pregnancy and lactation with no contraindications.

References to “Withdrawal Syndrom” Risk Development

The drug does not have "withdrawal syndrome".

Special Instructions

Does not affect the ability to drive or work with machines.

Overdose

Ga-40, a 40-fold therapeutic dose is completely safe for the body.

Drug Interactions

Compatible with all the drugs that are used in the above-mentioned diseases.

Condition and Term of Storage

It should be stored in a place protected from light at a temperature from +10 to 20°C.

Shelf Time

1 month after opening. 2 years unopened.

Pharmacy Issuing Rule

Obtained a prescription.

Manufactured by JSC “Biochimpharm” for “Alexis” LTD
3, Gotua Str., Tbilisi,