

## The medicinal product **TAMERON**<sup>®</sup> is your way to live a longer and healthier life

### Medicine «TAMERON<sup>®</sup>»

The medicine «**TAMERON**<sup>\*</sup>» is a synthetic low-molecular immunomodulator, the main active ingredient of which is aminodihydrophthalazindione sodium salt.

Medicinal product **«TAMERON**<sup>\*</sup>» has immunomodulatory, anti-inflammatory, antioxidant, antibacterial, antiviral, radioprotective, antifungal, regenerating, neuroprotective, analgesic, antitumor, geroprotective actions. Prescribed in the complex therapy of immunodeficiency conditions, viral hepatitis, diseases caused by herpes and human papilloma viruses, for acute, chronic infectious and inflammatory diseases of the gastrointestinal tract, genitourinary system, respiratory tract and ENT organs.

The effectiveness of the drug is confirmed by many years of research on the active substance – sodium aminodihydrophthalazindione. Clinical studies are ongoing and now we can say that the drug **«TAMERON**<sup>•</sup>» can reduce the time of illness and the severity of the disease.

**«TAMERON**<sup>®</sup>» is compatible with almost any medicine. The use of the drug allows you to reduce the dosage of non-steroidal and steroidal anti-inflammatory drugs and antibiotics.

Scientists have proven the extremely low toxicity of sodium aminodihydrophthalazindione (safe in doses of 275 mg per kg of body weight, LD50) and have established the effectiveness of high doses of up to 2 g per day in the treatment of chronic toxic brain damage caused by toxic substances.

The production technology of the **«TAMERON**<sup>\*</sup>» ensures the production of a highly purified and safe drug [22]. According to the results of recent Russian studies, **TAMERON**<sup>\*</sup> is quickly eliminated from the body and is non-toxic (safe in doses of more than 1000 mg per kg of body weight, LD50).

#### Fundamentals of fundamental and applied research of the drug aminodihydrophthalazindione sodium (TAMERON<sup>°</sup>) as a potential drug for the prevention, treatment and rehabilitation of patients with COVID-19

aminodihydrophthalazindione (sodium salt of luminol ) has been known as a medicine since 1997 (RU 97/91/3 dated March 31, 1997). It is manufactured under the Tamerit <sup>°</sup> and Galavit <sup>°</sup> trademarks . In November 2020, the **«TAMERON**<sup>°</sup>» was registered in the form of a lyophilisate for the preparation of a solution for intramuscular administration. The basis of the drug is a polyfunctional chemically pure synthesized compound - sodium aminodihydrophthalazindione [1, 2, 3, 4, 22, 25].

During the development of the method and technology for lyophilization of the «TAMERON», it was possible to achieve stabilization of the crystalline composition of the drug in the forms LOHKOK01 and LOHKOK02. In the early known drugs - Galavit <sup>°</sup> and Tamerit <sup>°,</sup> the percentage of these forms differs from **TAMERON**°. Therefore, it can be argued that, despite the fact that Galavit<sup>\*</sup>, Tamerit<sup>\*</sup> and TAMERON<sup>\*</sup> are similar pharmacological drugs, the difference in the content of crystalline forms in their compositions may indicate differences in some physicochemical and pharmacological properties of the drugs. Currently, active research is underway on dosage forms of sodium luminol abroad. In particular, the Swiss company Metriopharm has patents for the use of sodium luminol (it goes under the code name MP1032) for the treatment of: multiple sclerosis; acute pneumonia (as an aerosol form). This company also conducted research on dissolving sodium luminol in various co-solvents to make it possible to produce various dosage forms of this substance. The same company is conducting clinical trials of sodium luminol for the treatment of chronic psoriasis and coronavirus infection.

Thus, the history of the study of sodium luminol as a chemical substance and as a substance with pharmacological properties shows not only the development of knowledge and ideas about it as a medicinal product, but also outlines further ways to create new dosage forms with new properties and the use of this substance in medicine and biology

Based on the studies conducted, the described indication for the use of the drug comes down to a wide range of effects on the immune system [15, 18, 23, 24].

It is indicated that the drug aminodihydrophthalazindione sodium is able to regulate the activity of immune cells - monocytes, macrophages, neutrophils, natural killer (NK) cells responsible for different types of immunity. It has been shown that it normalizes the phagocytic activity of the monocyte-macrophage system, the bactericidal activity of neutrophils and the cytotoxic activity of NK cells.

The drug increases the body's resistance and reduces the severity of the disease caused by a viral, bacterial or fungal infection. It has been established that sodium aminodihydrophthalazindione normalizes the process of antibody formation and regulates the production of endogenous interferons (IFN-a, IFN-g) by cells. It has been shown that in the case of an inflammatory reaction, the drug can reversibly (for 6–8 hours) inhibit the excessive synthesis of TNF-a, IL-1, IL-6 and other proinflammatory cytokines by hyperactivated macrophages.

It was shown for the first time that sodium aminodihydrophthalazindione is able to suppress the generation of reactive oxygen species and exhibit antioxidant activity. During preclinical and clinical trials, it was found that the drug was well tolerated and had no allergenic, mutagenic, embryotoxic, teratogenic or carcinogenic effects. Comprehensive studies of the active pharmaceutical substance aminodihydrophthalazindione sodium and the drug **«TAMERON**<sup>\*</sup>» were carried out, which showed its active immunotropic effect [16]. Further work by researchers studying sodium aminodihydrophthalazinedione demonstrated more detailed mechanisms of its activity, which allow us to consider the drug **«TAMERON**<sup>\*</sup>», based on it, as a potential treatment for coronavirus infection.

## Aminodihydrophthalazindione, effect on the replication phase of the virus.

Viruses, when entering host cells, use several strategies for survival, including modulation of intracellular redox balance [23]. An imbalance of redox potential in an oxidant- rich environment is a key event in viral infections [31]. Many viruses induce oxidative stress, which is caused by excessive production of reactive oxygen species (ROS) and decreased levels of reduced glutathione, the main intracellular antioxidant, and such conditions promote viral replication [27].

It has been shown that the effect of the drug is due to its antioxidant effects and ability to activate the antioxidant defense system on level of gene expression by stabilizing the transcription factor Nrf 2 [32, 36]. This transcription factor is interesting in that it interacts with the promoter regions of ARE (antioxidant response element) on genomic DNA, which leads to activation of transcription of genes of various antioxidant systems (glutathione peroxidase, NADPH-quinone reductase, etc.). In addition, Nrf2 also interacts with the XRE promoter region (xenobiotic response element), which is accompanied by activation of the expression of xenobiotic metabolism enzymes [28]. As was later established, this transcription factor is activated when cells are damaged by other viruses (hepatitis, influenza and HIV viruses), while Nrf2 is an important part of intracellular antiviral activity, suppressing virus replication at the level of regulation of the redox state of cells [27]. It is worth noting that stabilization and the activity of

the transcription factor Nrf 2 ensures the preservation of the viability of astrocytes and microglia And neurons themselves under various dysfunctional conditions [29]. Studies of aminodihydrophthalazinedione sodium on a model of cultured astrocytes infected with the Moloney leukemia virus showed that viral cell damage is accompanied by the development of oxidative stress, and the presence of the drug activates the transcription factor Nrf2 and the genes regulated by it [34]. This promotes cell survival and slows down neurodegenerative processes in virus-infected animals [35]. Recently, using the example of rats in which neurogenic stress was induced as a model by permethrin , it was demonstrated that the use of sodium aminodihydrophthalazinedione leads to the restoration of the redox balance of nervous tissue cells. It reduces neuroinflammatory responses and stimulates neurogenesis in the hippocampus [37].

Replication and formation of new coronavirus viral particles in the cell is accompanied by the development of redox imbalance, which is one of the factors contributing to virus reproduction [7]. As in the case of other viral infections, activation of the transcription factor Nrf2 during coronavirus infection significantly reduces the cytopathicity of the virus, and this transcription factor can serve as one of the targets of pharmaceuticals that will alleviate the course of the infection and minimize complications [30]. Taking into account the molecular mechanisms of the activity of aminophthalazinedione sodium described above, its use (in the case of coronavirus infection) will normalize the redox potential of infected cells and thus prevent the replication of the virus and the development of cytopathic effects.

Consequently, the drug **«TAMERON**<sup>\*</sup>» Due to the chemical reaction, the ability to neutralize reactive oxygen species, which are inducers of inflammatory processes and the production of pro-inflammatory cytokines, is retained, which makes it possible to use it for the treatment of acute distress syndrome in severe cases of coronavirus infection COVID-19 [6]. Recently, quite a lot of studies have appeared on the neurogenic course of the COVID-19 disease, which describe the observed effects of damage to the central nervous system (symptoms similar to intracranial infection, meningitis, encephalopathy) and the peripheral nervous system (in most cases, anosmia). Since sodium aminodigdrophthalazindione exhibits protective and antioxidant effects at the level of nervous tissue cells, it can be assumed that the use of the drug will provide a neuroprotective effect and reduce the level of side effects and their severity associated with damage to the human nervous system by COVID-19.

# Aminodihydrophthalazindione and cytokine storm during coronavirus infection.

As mentioned above, the process of development of infection caused by SARS-CoV-2 is accompanied by the generation of reactive oxygen and nitrogen species, which is accompanied by a large release of cytokines (" cytokine storm"), a massive immune response in the body and extensive tissue damage [7]. In parallel, tissue damage by the COVID-19 virus leads to a decrease in interferon production, and this process enhances cytopathic effects and increases sensitivity to microbial threats [12, 17, 21]. At the same time, a decrease in the number of lymphocytes in the blood, in particular T-lymphocytes, can be observed [12]. Model experiments revealed that a decrease in the number of lymphocytes in the blood may be associated with infection of T cells by the SARS-CoV-2 virus, and the penetration of the virus into these cells occurs through active nonspecific endocytosis of viral particles, which is in no way associated with the ACE2 protein [39]. These phenomena reduce the ability of the immune system to resist infection, which can lead to exacerbation of the disease. The developing cytokine reaction can be successfully suppressed by the use of sodium aminodihydrophthalazinedione, which, due to its effect on the expression of antioxidant defense genes, significantly reduces the level of ROS generation. It is known that the generation of ROS during various types of infectious diseases and pathogenesis may be the cause of the subsequent production of proinflammatory cytokines. It is obvious that the antioxidant activity of the drug **«TAMERON**<sup>\*</sup>» and is the reason for its ability to reduce the level of synthesis of pro-inflammatory cytokines TNF-a, IL-1, IL-6 and suppress hyperinflammatory processes.

During studies of the biological activity of aminodihydrophthalazindine sodium using a mouse model infected with T- tropic cytopathic retrovirus, it was found that this drug interferes with viral replication, stabilizes the cytoskeleton thymocytes. This significantly reduces apoptosis and death of thymocytes during virus infection [36]. Based on these data, it can be argued that sodium aminodihydrophthalazinedione will contribute to the preservation of thymocytes even if they are damaged by coronavirus.

In addition to the indirect activation of the monocyte-macrophage system by cytokine signals, during COVID-19 infection the virus is able to infect macrophages. It has been shown to be endocytosed by macrophages, which are attracted in large numbers by alveolar epithelial cells released by chemoattractants . The virus that has penetrated macrophages activates inflammatory genes and systems for the production of reactive oxygen species and phospholipid peroxidation , which leads to total oxidative stress in the area of the alveoli and their environment [33]. It is assumed that activation of oxidative stress of macrophages by the virus, through the generation of oxidized phospholipids and their effect on the production of tissue factor CD142 (or coagulation factor III) in capillary endothelial cells, may contribute to one of the key pathological processes during COVID-19 infection— thrombosis in lung tissue. That is why the use of the drug **«TAMERON**<sup>\*</sup>» based on aminodihydrophthalazinedione sodium allows you to directly stop the oxidative stress developed by macrophages during coronavirus infection, will help prevent massive thrombus formation and preserve the lung alveoli from destruction.

Therefore, the drug **«TAMERON**<sup>\*</sup>» prevents the proliferation of the virus, promoting the preservation of alveolar and other cells of the body, including immune cells (in particular, monocytes and T-cells), and also activates a response at the level of T-lymphocytes, which lyse body cells infected with the virus [7].

Thus, there is scientific evidence that the use of the drug «TAMERON<sup>\*</sup>», in the prevention and treatment of acute viral infections including SARS-CoV-2, can reduce oxidative stress in cells and tissues, inhibit the development of a cytokine storm and hyperreaction of the immune system, and prevent reproduction of the virus, promote the preservation of alveolar cells and other cells of the body, and also activate subpopulations of T-lymphocytes aimed at the formation of specific immunity and neutralization of the virus.

**TAMERON**<sup>®</sup> can also successfully prove itself in the treatment and rehabilitation of neurogenic pathological processes associated with coronavirus infection.

#### Clinical testing of the drug «TAMERON<sup>®</sup>» for the prevention of COVID-19

A drug based on sodium aminodihydrophthalazinedione has shown high effectiveness as a means of prevention in a difficult epidemiological situation regarding the incidence of COVID-19 and during the period of rising incidence of influenza, including the H  $_1$  N  $_{\rm 1\,strain}.$ 

The drug was used for prophylactic purposes in a 15-day course with a single, 100 mg intramuscular, daily administration to military

personnel aged 50 to 60 years, who were daily for a long period of time in contact with persons who had, or subsequently developed, symptoms of acute respiratory infections. viral infections. In this category, neither subjective nor objective manifestations of infectious diseases were identified [20].

#### Possible options for prescribing the drug sodium aminodihydrophthalazinedione (TAMERON<sup>°</sup>) in the prevention of COVID-19:

For adults, the drug dosage regimen for prophylactic purposes is 100 mg intramuscularly once a day for 15 days.

The effectiveness of the drug with other administration regimens has not been studied.

#### Clinical testing of the drug **«TAMERON**<sup>®</sup>» (aminodihydrophthalazinedione sodium) in the complex treatment of patients with COVID-19

Currently, a study is ongoing in which the scientific implementation of inpatient treatment methods using the drug **«TAMERON**<sup>\*</sup>» was carried out 100 mg intramuscularly once a day for 7 days in standard therapy for children with moderate COVID-19. This is a prospective comparative non-randomized a single-center observational study to evaluate the effectiveness of the drug **«TAMERON**<sup>\*</sup>» in the form of an injection in the treatment of moderate coronavirus infection in children aged 6 to 12 years. The severity of the coronavirus infection is determined by the research physician based on current clinical recommendations.

The prescription of an immunoprophylaxis regimen for complications of moderate coronavirus infection when using **TAMERON**<sup>°</sup> in children aged 6 to 12 years in a hospital is made at the discretion of the researcher in the form of an injection in accordance with local clinical practice and/or instructions for medical use.

If parents refuse immunoprophylaxis for complications of moderate coronavirus infection using the drug **«TAMERON**<sup>°</sup>», they are offered to participate in the study in the control group without immunoprophylaxis. Thus, the study formed two groups of patients aged 6 to 12 years for observation: group 1 – patients receiving **TAMERON**<sup>°</sup> for immunoprophylaxis, one injection of 100 mg daily for 7 days in the hospital; group 2 – patients not receiving **TAMERON**<sup>°</sup> for immunoprophylaxis (control group).

The study participant is observed for 90 days, during which the necessary data is collected.

After the patient is included in the study, data is collected on gender, age, complaints at the time of examination, anamnesis of the present disease, general examination data, concomitant diseases/ conditions, previous surgical interventions, and this data is entered into an individual registration card (IRC). In addition, the researcher enters into the CRF data on the medications used in the patient to treat coronavirus infection and concomitant diseases/conditions.

When a patient is included in the study, a laboratory examination is carried out - a clinical blood test (hemoglobin level, erythrocytes, platelets, leukocytes, leukocyte formula, absolute number of band and segmented neutrophils, absolute number of lymphocytes, absolute number of monocytes, absolute number of eosinophils, absolute number of basophils, sedimentation rate erythrocytes), clinical urine analysis (relative density, protein level, glucose level, leukocyte count, erythrocyte count, data on bacteria in sediment), biochemical blood test (level of C-reactive protein, total and direct bilirubin, creatinine, triglycerides , ferritin , ALT, AST, LDH, creatine phosphokinase , troponin, K+, Na +, Mg2+, Ca2+ ions , procalcitonin ), coagulograms (level of fibrinogen, D- dimer , thrombin time, activated partial thromboplastin time), molecular biological diagnosis of COVID-19 using the polymerase method chain reaction (nasal or oropharyngeal swabs). The described laboratory examination of the patient is repeated on days 5 and 10 of the observation period. Additionally, upon inclusion in the study and after 10 days, an immunological blood test is performed (phagocytic activity of neutrophils, phagocytosis completion index, number of active phagocytes, T-lymphocytes (CD3+), T-helpers (CD4+), T-cytotoxic cells (CD8+), B- lymphocytes (CD19+), immunoregulatory index (CD4/CD8), circulating immune complexes, immunoglobulins M (IgM) and G (IgG) to SARS-CoV-2.

When a patient is included in the study, an instrumental examination is carried out during the observation period - ECG, spiral computed tomography of the chest, ultrasound of the heart. Ultrasound of the abdominal cavity and ECHO CG are performed according to indications. On days 5 and 10, studies are carried out according to the decision of the research physician if there are indications for assessing the end points of the study.

On the 90th day of the observation period, the researcher analyzes the number and reasons for the patient's visits to medical institutions in a unified medical information and analytical system. If necessary, it is possible to conduct an unscheduled visit to the patient on any day of the observation period to assess the end points of the study.

Preliminary results of the study showed that the use of the drug increased the activity of cellular and humoral immunity. The number of circulating immune complexes, which reflect the activity of the infectious process in the body, decreased with the use of the drug **«TAMERON"**» compared to the control group of patients.

The drug **«TAMERON**<sup>®</sup> had a positive effect on clinical indicators, reducing the duration of the period of increased body temperature above 37C<sup>0</sup>, intoxication and catastrophic syndromes. The temperature has returned to normal for the 4th day. Peripheral blood analysis showed normalization of leukocyte levels and ESR at the time of discharge.

Consequently, the use of the drug in complex treatment in patients with mild and moderate forms of COVID-19 led to a decrease in the severity of the disease, acceleration of recovery, a decrease in the level of antibiotic consumption and the frequency of disease relapses [19].

Based on clinical and methodological materials, **TAMERON**<sup>\*</sup> is included in the clinical protocol for the treatment of children with a new coronavirus infection (COVID-19) who are undergoing inpatient treatment in medical organizations of the state healthcare system of the city of Moscow.

#### Possible options for prescribing the drug aminodihydrophthalazinedione sodium (TAMERON<sup>°</sup>) in complex treatment patients with COVID-19:

According to the results of the above study, in children who were hospitalized with a diagnosis of a new coronavirus infection of moderate severity, the drug aminodihydrophthalazinedione sodium may be included in standard therapy in accordance with the temporary clinical recommendations of the Ministry of Health of the Russian Federation with the use of injection forms of use of the drug «TAMERON<sup>®</sup>» 100 mg intramuscularly 1 time per day for 7 days.

Studies using the drug aminodihydrophthalazinedione sodium in standard treatment in adults in the treatment of COVID-19 continues.

#### Immunosuppressive therapy during the rehabilitation period of COVID-19

In post-Covid syndrome, as in COVID-19, the regulation of the ratio of reproduction and degradation of transcription factors is disrupted. There is an inversion in the work of protective cascades despite cell damage and the development of oxidative stress, instead of NRF2 activation, hydrolysis and suppression of NRF2 synthesis are observed. As a result, the level of the anti-inflammatory factor NRF2 sharply decreases, and the expression of the pro-inflammatory factor NF- kB increases . A decrease in the level of NRF2 is the pathogenetic basis for the use of TAMERON [9, 14].

### **Perspectives on clinical practice**

#### Radioprotective properties of sodium aminodihydrophthalazinedione drug

Recent studies reveal new mechanisms of action of sodium aminodihydrophthalazinedione. Studies have shown that the drug helps maintain the viability of normal cells, but at the same time promotes the death of cancer cells under ionizing radiation. The presence of the drug in healthy cells when exposed to ionizing radiation prevents the development of oxidative stress, reduces the level of lipid peroxidation of cell membranes, accelerates DNA repair after damage, promotes the preservation of the activity of genes responsible for antioxidant protection, preservation of proliferative activity and regulation of the cell cycle. In cancer cells, the drug **«TAMERON**<sup>•</sup>» does not exhibit radioprotective properties, but on the contrary, against the background of ionizing radiation, it accelerates the development of oxidative stress, DNA damage and arrest of the cell cycle of cancer cells [8, 38].

Testing the radioprotective properties of the drug in doses of 300 and 500 mg/kg on a model of white SHR mice demonstrated an increase in animal survival by 20%, a 2.5-fold reduction in the severity of early leukopenia, and accelerated skin wound repair on day 8, which indicates its anti-radiation effectiveness with combined radiation-mechanical injuries [11].

#### Geroprotective properties of the drug aminodihydrophthalazinedione sodium

A number of studies on primates have found that the drug can improve blood counts and testosterone levels to the level of younger animals, and also maintain low levels of the indicator oxidative stress for a long time (about a year) [10, 26].

Preliminary results from other work show that the drug in aging stem cells promotes longer preservation of the activity of the telomerase enzyme and preserves longer telomeres, and the cells themselves retain signs of stemness for a longer time and have lower labeling patterns compared to cells not treated with the drug (on Research is currently ongoing).

In a rat model of permethrin- induced neuroinflammation, the use of a drug containing sodium aminodihydrophthalazindione significantly reduced the development of oxidative stress in neurons and glia of the animal's brain and activated the expression of antioxidant defense genes. Animals treated with the drug demonstrated better cognitive functions, the development of anti-inflammatory and proneurogenic effects was observed due to a decrease in the density of hypertrophied astrocytes and activated microglia, as well as increased neurogenesis with increased proliferation of neural stem cells. Moreover, the use normalized the concentration of many pro-inflammatory markers in the circulating blood (research is ongoing).

Studies have been conducted on the effect of sodium aminodihydrophthalazinedione on the course of Parkinson's disease using a rat model. The use of the drug restored redox processes in the brain of experimental animals, as well as in the circulating blood. A decrease in the level of inflammatory processes and systemic inflammation, an improvement in neurogenesis in the brain, cognitive functions, and mood were also observed [37]. Thus, the drug **«TAMERON**<sup>\*</sup>» in the future, it can be used as an effective neuroprotective and anti-neuroinflammatory drug, allowing to preserve brain neurons from damage in various diseases associated with neuroinflammation (Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, etc.) and preserve cognitive abilities, including in patients with post-Covid syndrome, and the drug can also be used by military personnel as a preventive and medicinal agent to normalize the redox balance, prevent the development of inflammation in the nerve cells of the brain, which in turn will be accompanied by greater human resistance to stress factors, increased cognitive functions of the brain in stressful situations situations [5].

National Medical Research Center of Traumatology and Orthopedics named after N.N. Priorov, a positive effect was established when studying the effect of the drug **«TAMERON**<sup>•</sup>» for infectious complications during spinal surgery, joint replacement and treatment of osteomelitis.

On the basis of the City Clinical Hospital named after. M.P. Konchalovsky conducted research on the use of the drug **«TAMERON**<sup>\*</sup>» to prevent the development of infectious complications (suppuration) in patients with 2 or more competing diseases (diabetes mellitus (required), rheumatoid arthritis, systemic lupus erythematosus, systemic scleroderma, etc.). Studies have shown that the drug increases the activity of cellular and humoral immunity and reduces the length of hospital treatment.

We also assessed the effectiveness of the drug **«TAMERON**<sup>®</sup>» in improving the treatment of purulent soft tissue diseases in the treatment of patients with viral hepatitis (hepatitis B and C) and/or HIV infection who are not receiving antiretroviral therapy.

The use of the drug «TAMERON<sup>®</sup>» increases the activity of cellular and humoral immunity in patients suffering from purulent diseases of soft tissues, with viral hepatitis (hepatitis B and C) and/or HIV infection who are not receiving antiretroviral therapy. This fact is confirmed by the results of the study: patients in the experimental group showed an increase in the activity of T-lymphocytes, T-helpers, B-lymphocytes, natural killer cells, activated lymphocytes and the level of immunoglobulin G 10 days after the start of treatment with the drug. In the control group, the picture did not change during treatment.

When studying the clinical effectiveness of the drug **«TAMERON**<sup>\*</sup>» for vertebrogenic neuropathic pain in patients with diseases (M40-M54) and injuries (S12-S32) of the spine, it was found that the drug is safe and effective, can be used as a second-line drug for combination treatment, a significant decrease in the level of pain was noted in the VAS score for radicular leg pain, increased level of mental health when assessed by SF-36 compared to the control group.

#### product «TAMERON<sup>®</sup>» is recommended:

• **Federal Medical and Biological Agency** methodically: for the prevention and treatment of influenza and other acute respiratory viral infections;

• **Department of Health of the City of Moscow** clinically: for the treatment of children with a new coronavirus infection;

• Federal State Budgetary Educational Institution of Higher Education «Krasnoyarsk State Medical University named after Professor V.F. Voino-Yasenetsky « of the Ministry of Health of the Russian Federation and the Research Institute of Medical Problems of the North of the Federal State Budgetary Institution «Federal Research Center Krasnoyarsk Scientific Center of the Siberian Branch of the Russian Academy of Sciences» educa*tional and methodological* : for the immunorehabilitation of patients who have suffered Covid-19.

#### **Results of scientific and clinical studies of the drug «TAMERON**<sup>®</sup>» over the past three years:

• reduces the number of infectious complications during spinal surgery, joint replacement and treatment of osteomyelitis when used prophylactically TAM-ERON (N.N. Priorov National Medical Research Center );

• reduces the length of hospital treatment in patients with diabetes mellitus and at least two competing diseases (M.P. Konchalovsky City Clinical Hospital );

• increases the effectiveness of treatment of purulent diseases of soft tissues in the treatment of patients with viral hepatitis (hepatitis B and C) and/or HIV infection who are not receiving antiretroviral therapy (M.P. Konchalovsky City Clinical Hospital);

• reduces the risk of developing purulent-septic complications during endoprosthetics and treatment of osteomyelitis (N.N. Priorov National Medical Research Center for Orthopedics and Orthopedics );

• Research continues on the effect on the antibacterial sensitivity of microorganisms with the combined use of antibiotics and TAMERON (Research Institute of Medical Problems of the North, Federal Research Center Krasnoyarsk Scientific Center of the Siberian Branch of the Russian Academy of Sciences).

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