

INSTRUCTION
for medical usage of the preparation:
“ERBISOL” solution for injections
(ERBISOLUM pro injectionibus)

GENERAL CHARACTERISTIC:

International name: Erbisol.

Principal physical and chemical properties: transparent colourless or light yellow liquid;

composition: a complex of the natural protein-free low-molecular weight organic combinations of nonhormonal origin obtained from the embryonic tissue of chicken or duck germs, contains glycopeptides, peptides, nucleotides and amino acids.

FORM OF OUTPUT. Solution for injections.

PHARMACOLOGICAL GROUP.

Cytokines and immunomodulators. Code ATC L03A X.

Hepatotropic preparations. Code ATC A05B A.

PHARMACOLOGICAL CHARACTERISTICS. *Pharmacodynamics.* Pharmacological activity of the medication is determined by the content of low-molecular weight biologically active peptides, activating the natural evolutionally formed controlling systems, responsible for the search and elimination of pathological changes in the organism. Erbisol makes more activates the immune system for the accelerated restoration of the cells damaged, and the destruction of anomalous cells and tissues. A principal immunomodulating effect of the medication is first of all realized throughout its effect on macrophagic link, responsible for repair of the damaged cells and the restoration of organ and tissue functional activity, and throughout N- and T-killers, which are responsible for the destruction of damaged cells, incapable for the regeneration, or anomalous cells (mutant, malignant, virus carrying cells and so on) and tissues too. Further more, Erbisol has the immunocorrelating action and promotes the normalization of disturbed immunologic status by activating T-lymphocytes, Th1-helpers and T-killers and inhibiting the activity of Th2-helpers and B-lymphocytes that is important for the balance recovery between cellular and humoral immunity in oncologic diseases, and for stopping the autoimmune processes. Depending on the immune status of the organism the medication corrects the activity of some other factors in the cellular and humoral immunity, induces the synthesis of α -, β -, γ -interferons and tumor necrosis factor. Erbisol potentiates the effect of antibiotics, exogenous interferons and decreases their toxic side effect.

Erbisol accelerates the regenerative and reparative processes in patients with erosive

gastric intestinal ulcers, contributes to healing the mucosal damage in the stomach and duodenum. The medication increases regenerative and reparative tissue potential, resulting in healing of trophic ulcers, traumatic, postoperative and pyoceptic wounds, traumas and also the consolidation of osseous breakings in fractures, the treatment of parodontitis and paradontosis.

Erbisol effectivity was revealed at the treatment of acute and chronic hepatitis of various aetiology including toxic, medicamentous and virus hepatitis while the preparation activates the regenerative processes of the liver. In virus hepatitis Erbisol makes more active T-killers for destroying the cells of virus carrier and also induces the synthesis of α - β - and γ -interferons increasing their blood level in 4-6 times that contributes the accelerated virus elimination additionally. At the same time, while activating the regenerative processes of the liver the medication promotes the substitution of dead hepatocytes by healthy ones, that allows Erbisol to be related to the medications, decreasing the severity of infectious disease. The medication has antiinflammatory properties, however the treatment of chronic inflammatory processes may be without the acute phase during 2-5 days. Erbisol contributes to the normalization of the hepatocyte functions, it manifests the clear antioxidant and membranostabilizing effects at the level of plasma membranes, prevents the development of dystrophy, cytolysis, cholestasis and also atherosclerosis in the liver damages, contributes to the normalization of the bilirubin and transaminase levels. All this leads to quicker disappearance of asthenovegetative, dispeptic and painful syndromes. Making more active the liver functions the preparation promotes the accelerated elimination of foreign toxic agents and injurious products of the organism vital activity.

At the chronic obstructive lung diseases and bronchial asthma with respiratory deficiency, Erbisol decreases neutrophile inflammation, which excessive activation creates an irreversible component of bronchial obstruction by the destruction of elastic collagen base of the lungs. The decrease in cellular inflammation contributes to functional improvement of external respiration, that influences on the level of tissue hypoxia, energy supply of cells, to the decrease of toxin contents in their membranes and immunocomplexes, potentiates catecholaminebinding function of erythrocyte membranes, decreases the relative viscosity of erythrocyte suspension and capacity for red blood cell aggregation, increases the erythrocyte deformity that promotes the increase in blood dilution and the improvement of microcirculation. Clinical effect of Erbisol is manifested by the significant weakening of expressed cellular symptoms of disease, the positive increase in dynamic indices of functional external respiration, decrease in a number of inhalation bronchodilators, that are used.

In insulin dependent diabetes mellitus (type 1 diabetes mellitus) Erbisol inhibiting the activity of Th2-helpers, decreases the intensity of autoimmune processes, and activating

macrophages, contributes to the reparation of damaged beta-cells, that leads to a decrease in daily requirement of insulin injections, and also to the stable compensation of carbohydrate and lipid metabolism, to the decrease in lipid peroxidation. This contributes to the decrease or liquidation of clinical signs and to the functional improvement of the liver, myocardium, cardiovascular system. In complex therapy Erbisol has the positive effect on the treatment of neuropathy, macro- and microangiopathies in diabetes mellitus; improves the microcirculation of the blood vessels, prevents the development of gangrene. In newly diagnosed diabetes mellitus Erbisol contributes to the significant decrease in daily dose of insulin, to the persistent and prolonged remission. In patients with non insulin dependent diabetes mellitus (type 2 diabetes mellitus) Erbisol regulates the indices of metabolic syndrome, and improves myocardial contractility. Erbisol contributes to the improvement of life level in patients with diabetes mellitus.

In oncologic patients, ERBISOL does not stimulate their disbalanced immune system, but first of all promotes its correction, normalizing the immune status by activation of T-lymphocytes, Th1-helpers and T-killers, inhibiting of Th2-helpers and B-lymphocytes, that contributes to the restoration of specific cell immunity and first of all to the activation of T-killers, in contrast to other immunomodulators. The medication also activates the macrophages and natural killers (N-killers) of unspecific immunity, induces the synthesis of α - and γ -interferons and factor of necrotic tumours. This leads to inhibition of the malignant tumor growth and metastasis, and in a case of a complex surgical intervention or chemo- and radiotherapy contributes to their effective destruction. As a medication of accompaniment for chemo- and radiotherapy, Erbisol, significantly increases an efficacy of the treatment in two directions: **firstly**, as the reparant, hepato- and immunoprotector it protects the healthy cells and tissues from chemical and radiation injuries, restoring the damaged links. This allows to apply more intensive regimens of drastic chemical preparations and radiation doses without the risk for arising the significant negative consequences in patient status, preventing the loss of hear, elimination or significant decrease in the manifestations of vegetative, dyspeptic and painful syndromes. **Secondly**, as immunocorrector the medication restores the antitumorous functions of the immune system and despite a damaged effect of chemo- and radiotherapy contributes to the normalization of immune status in patients after the treatment to the parameters, comparable with the parameters of immune status of healthy persons. This permits to mobilize the protective antitumorous functions of the organism during the treatment, as well as between the periods of treatment courses, that favour their increased role, and an improvement of the living standard and also the possibile substitution of some chemotherapy courses by immunotherapy and immunocorrection with Erbisol, in contrast to the standard chemo- and radiotherapy. A decrease in a number of the repeated intensive courses of chemo- and radiotherapy, that

were needed in nearest period and also the decrease in the incidence of newly diagnosed metastatic nodes in the periods between the plan courses of treatment were revealed by clinical examinations in patients, who applied Erbisol.

Erbisol is a **adaptogene**, increasing the protective and adjusting functions of organism. Its use is recommended for the complex therapy in the treatment of consequences of radiation effect and ecological contaminations. The medication manifests the radioprotective effect, associated with its membranostabilizing and antioxidant properties, the activation of reparative processes at the cellular as well as genetic (activizes DNA-polymerase-B – a reparant of genetic code) levels, the normalization of the liver functions for effective elimination of the alien toxic agents.

Erbisol activates the immune system for inspection and restoration of the organism, that is of great importance in gerontology, as in the process of vital activity a great number of the anomalous cells are accumulated, many of which are in the “drowsiness” state and are activated while the immune system is relaxed. Erbisol contributes to the functional rehabilitation of the immune system, when activated N- and T-killers have opportunity for the inspection (to find and destroy the anomalous cells and to do any restoration of macrophages), for the regeneration of organ and tissue functions disturbed in elderly patients.

The medication is nontoxic, without the cumulative toxic, allergogenic, teratogenic, mutagenous and carcinogenous activities.

Immunomodulating effect begins to develop on the days 5-7 and maximum index is reached on the days 20-21 retaining more 8-10 days at the same level after finishing the medication administration. The reparative effect begins to develop on the days 2-3 of the treatment and the hepatoprotective effect is manifested after 2-3 injections of the medication.

Pharmacokinetics. It is not studied.

INDICATIONS:

- **Gastroenterology:** hepatitis of various aetiology (including virus, toxic and also medicamentous hepatitis provoked by the usage of antibiotics, interferons, chemicals and other drastic medicamentous preparations inducing side effects), hepatopathies, hepatitis, hepatic cirrhosis, stomach and duodenum ulcers, erosive gastroduodenitis, ulcerative colitis.

- **Toxicology:** Erbisol activates the desintoxication function of the liver;

- **Endocrinology:** diabetes mellitus, autoimmune thyroiditis.

- **Therapy:** nonspecific pulmonary diseases (pneumonia, chronic bronchitis), metabolic dystrophies, angiopathies; for the improvement of microcirculation, the normalization of tonus and bloodfilling of the vessels. Erbisol is applied in the complex therapy of patients, suffered as the result of radiation consequences and ecologic

contamination the preparation has pronounced adaptation-correlation characteristics increasing the compensatory and protective functions of the organism.

- **Allergology:** allergic and autoimmune diseases including bronchial asthma, atopic dermatitis, atopic rhino-conjunctivitis;

- **Gerontology:** in functional insufficiency, associated with the age disturbances in the liver, immune, nervous and cardiovascular systems. For increase the physical activity and potency, for the elimination of asthenic syndrome

- **Stomatology:** parodontitis and paradontosis.

- **Surgery and traumatology:** traumatic, postoperative and pyo-ceptic wounds, fractures (for accelerated consolidation of osteal breakings), trophic ulcers of different etiology, diabetic angiopathies, decubitus.

- **Oncology:** during a surgical treatment for prophylaxis of metastasis and for rapid healing of wounds (as a reparant). Erbisol is used in complex with chemo- and radiotherapy as a medication of accompaniment as a hepato-, immunoprotector and reparant, but during the rehabilitation period and the periods between the treatment courses is also applied as an immunoprotector and reparant for the activation of antitumor protection of the organism.

DOSAGE AND ADMINISTRATION: The medication Erbisol, solution for injections, is daily administered as intramuscular injection into the buttocks or intravenously or intraarterially of adults in a dose of 2-4 ml for 20 days treatment course. Taking into account the chronorhythms of the organism, its single administration is desirable in the evening at 20-22 o'clock before going to the bed in 2-3 hours after food, in a case of double administration an additional administration is needed at 6-8 o'clock, 1-2 hours before food if other times are not stipulated. The course dose consists of 40 - 80 ml.

At hepatopathies, exacerbation of inflammatory processes, autoimmune, allergic diseases Erbisol is daily administered of adults in a dose of 2 ml for 20 days.

At wounds, parodontitis and paradontosis Erbisol is administered of adults in a dose of 4 ml for the first 10 days, and in a dose of 2 ml for the next 10 days in a case of need. The additional gingival applications and electrophoresis with Erbisol from the (+) are applied in generalized paradontitis.

In patients with chronic obstructive lung diseases and bronchial asthma with respiratory deficiency of degree I Erbisol is administered in a single daily dose of 2 ml intramuscularly at 20-22 o'clock the first 3 days then twice daily at 17 and 20-22 o'clock for 5 days and then once daily at 20-22 o'clock for 7 days. The medication is alternatively administered in 2-3 hours after the food in both buttocks. The course dose consists of 40 ml. In chronic obstructive lung diseases and bronchial asthma with respiratory deficiency of

degree II the medication is daily administered intramuscularly at 20-22 o'clock for the first 3 days and twice a day - the next 10 days: in a dose of 2 ml intramuscularly at 17 and 20-22 o'clock, then in a dose of 2 ml intramuscularly at 20-22 o'clock for 7 days. The course dose consists of 60 ml. The requirement of Erbisol for the treatment course of chronic obstructive lung diseases and bronchial asthma accompanied by great and irreversible changes in the function of external respiration with respiratory deficiency of degree III is no less than 80ml. The medication is twice prescribed in patients of this group: in a dose of 2 ml intramuscularly at 17 and 20-22 o'clock for 20 days. The offered method of the treatment supplements the basic schema of therapy.

At hepatitis, hepatosis, hepatic cirrhosis, erosive ulcerous injuries of gastrointestinal tract, ulcerative colitis, metabolic dystrophies, tissue damages, trauma-tisms, fractures (for precipitation of the consolidation in the osseous breakings), trophic ulcers of different aetiology, decubitus and also for the quicker consolidation of osseous breakings, for the rehabilitation and reducing therapy, for increasing the physical activity and total vital tonus Erbisol is twice applied every day: in a dose of 2 ml at 6-8 and 20-22 o'clock for 20 days or in a single daily dose at 20-22 o'clock for the first 3 days. The next 10 days Erbisol is twice administered in a dose of 2 ml at 6-8 o'clock and at 20-22 o'clock and then in a dose of 2 ml at 20-22 o'clock for 7 days.

In diabetes mellitus, autoimmune thyroiditis Erbisol is preferably administered intravenously twice in a daily dose of 2 ml at 9-11 o'clock in the morning and at 20-22 o'clock in the evening for 20 days. The course of therapy may be repeated 2-3 times a year.

At oncologic diseases, as a medication of accompaniment and rehabilitation in radiotherapy Erbisol is twice applied in radiotherapy in a daily intramuscular dose of 2 ml at 6-8 o'clock in the morning and at 20-22 o'clock in the evening for 20 days starting course with 1-2 days before the radiotherapy.

In chemotherapy Erbisol is administered in a daily intramuscular dose of 2 ml at 20-22 o'clock in the evening starting with 2-3 days before, during the course of chemotherapy and finishing on the 7-12 days after chemotherapy (15-25 days) and also in a intramuscular dose of 2 ml starting with 1-2 days before, during the chemotherapy course and finishing on the days 3-7 after the end of chemotherapy. It means that Erbisol can be applied in a single daily dose of 2 ml at 20-22 o'clock in the evening on the first and the last 4-7 days of Erbisol course. On the days of chemotherapy Erbisol injection is applied in a fractional dose of 4-16 ml. It is advisable to administer Erbisol injection in a dose of 2 ml in the morning instead of the intramuscular (depending on dosage regimen of chemical preparations) directly before the administration of every cytostatic agents by intravenous, intraarterial, intratumorous or intraperitoneal injections and the additional intramuscular injection of Erbisol in a dose of 2 ml at 17 o'clock. For example, Erbisol is firstly administered intravenously in a dose of 2 ml

before the infusion of every 200 ml chemical solution as the intravenous drop infusion of chemical preparation. In regional chemotherapy Erbisol is administered in a dose of 4 ml by intraarterial or intratumorous injections before the administration of chemical solution by the same way. An additional intramuscular administration of Erbisol in a dose of 2 ml is prescribed in 2-3 days after the administration of acute doses of chemical preparations which accompaniment requires 8-16 ml Erbisol.

The calculation of Erbisol amount necessary for use in the complex with chemical preparations to prevent their side effects on patient healthy tissues, is realized depending on a injected dose of chemical preparations. For example, the administration of Erbisol in a dose of 2 ml is desirable before every: 25-30 mg of doxorubitsine or 25 mg of platinum agents or 0,5-0,75 g of cyclophosphane or 1,0 g of 5-fluoruratsile or other chemical preparations with an equivalent toxic effect.

Some examples of schemes for Erbisol use an accompaniment of chemotherapy courses are mentioned below in Appendix.

If the patient was underwent a surgical intervention before chemo- and radiotherapy, Erbisol is prescribed in a dose of 2 ml intramuscularly in the evening for 7-10 days before physical status the course of chemoradiotherapy starting from the days 1-3 after an operation. It is advisable for the patients with concomitant liver diseases and/or hepatitis in the anamnesis.

For improvement of patient physical status, a course of immunotherapy with Erbisol can be performed in 3-5 weeks after a chemotherapy. The first 3 days, Erbisol is intramuscularly taken in a single daily of adults dose of 2 ml at 20-22 o'clock in the evening. The next 5-10 days – twice a day: in a dose of 2 ml at 6-8 o'clock in the morning and at 20-22 o'clock in the evening, and then in a dose of 2 ml at 20-22 o'clock in the evening for 7 days.

SIDE EFFECT. Erbisol has a good tolerance in patients and the side effects are in the most cases absent. However, in some cases during the first days of the administration, the medication can induce an exacerbation of chronic inflammatory process that is not considered as a negative effect because this is a stage of curative process in the majority of cases.

CONTRAINDICATIONS: individual intolerance.

OVERDOSAGE. A short-term increased excitability can take place, which does not need specific therapy.

INTERACTION WITH OTHER MEDICINES. Erbisol potentiates the effect of antibacterial agents and interferons. For the effective realization of direct immuno-

modulating effect Erbisol is prohibited to use together with:

- a). **alcohol** (it neutralizes the reparative effect of the macrophages);
- б). **immunomodulators** that can stimulate the humoral immunity preventing the T-killer effect.

Erbisol increases the receptor sensitivity so its complex application with the hormonal medications, biostimulators and bioinhibitors (tranquilizers, soporific, ataraxic, psychotropic agents, depressants and so on) requires the control of their dosage and the decrease in a case of need.

PECULIARITIES OF USAGE.

CHOLECYSTITIS	It should be combined with therapy, normalizing the activity of the biliary system.
HYPERTENSION	Erbisol should be prescribed in a single 2 ml dose in the evening, in acute conditions of disease - a single 2 ml dose per day.
ULCEROUS the DISEASES	It is combined with erydical anticheliobacterial therapy. Under increased acidic production of the stomach antiseptants (blockators of H ₂ histamine receptors and proton pumps), antacid preparations are needed for usage.
D I A B E T E S M E L L I T U S	The blood sugar level should be controlled starting from the day 3 of preparation usage. In a case of its reduced, the insulin dose should be decreased. The level of blood sugar can be fluctuated at the first 10 -12 days, however a tendency to its decrease is then manifested, and the treatment course will be advisable to continue by 30 days in this case.

In increased blood pressure and also in the phase of acute pathologic processes the preparation should be used with care, decreasing a dose.

Erbisol should be prescribed under the doctor observation in the period of pregnancy, nursing and in children under 18 years.

CONDITIONS AND TERM OF STORAGE.

Keep the medication at a temperature of +4 - 12° C, keep the preparation out of the reach of children. Term of preservation is 5 years. An appearance of opalescence is permissible during storage.

TERMS OF DISTRIBUTION. According to prescription.

PACKING. 10 ampules per 1 ml or 2 ml.

MANUFACTURER. Scientific-Industry Centre "ERBIS" Ltd.

E-mail: erbis@ukr.net

Homepage: www.erbisol.com.ua

ADDRESS. Ukraine, 03113 Kiev, Dehtyarovsky Str., 53., tel: + 38 (044) 455-50-89.

Appendix

The examples of some schemes for Erbisol accompaniment of the chemotherapy courses during treatment of oncologic patients.

- A. A course of chemotherapy (CT) with fractional **intratumorous (i.t.)** administration of chemical preparations (CP).
90 mg of doxorubitsine + 90 mg of platinum .

1 amp1 1 1 1 1 / / / /

intramuscularly at $7 \pm 1,0$ o'clock
in the morning

CP	CP	CP
2	2	2

intratumorous administration
in combination with CT

1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 / / / / / /

intramuscularly at $17 \pm 0,5$ day-time
intramuscularly at $21 \pm 1,0$ evening

30 ampoules per 2 ml of Erbisol for 12 days (minimum),
or 40 ampoules per 2 ml of Erbisol for 18 days (optimum).

B. A course of chemotherapy with single intravenous (i.v.) administration of chemical preparations (CP) .

100 mg doxorubitsine + 1,5 g cyclophosphane.

1 amp1 1 1 1 / /	intramuscularly at $7 \pm 1,0$ morning		
<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td>CP</td></tr><tr><td>4-8</td></tr></table>	CP	4-8	intravenous administration
CP			
4-8			
	in combination with CT		
1 1 1	intramuscularly at $17 \pm 0,5$ day-time		
1 1 1 1 1 1 1 1 1 1 / /	intramuscularly at $21 \pm 1,0$ evening		

30 ampoules per 2 ml of Erbisol for 13-15 days.

Note: 1 – obliged administration of Erbisol
/ – desirable administration of Erbisol.

C. A course of chemotherapy (CT) with fractional intravenous (i.v.) administration of chemical preparations.

I. 40 mg of doxorubitsine+2,0 g of vincristine+1,0 g of cyclophosphane;

I. 40 mg of doxorubitsine+2,0 g of vincristine+1,0 g of cyclophosphane
15 mg of bleomitsine;

+10-

III. 10-15 mg of bleomitsine.

1amp.1 1 1 1 1 1	1 1 1 1 1 1	1 1 1	intramuscularly at $7 \pm 1,0$ morning						
<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td>CP</td></tr><tr><td>4-6</td></tr></table>	CP	4-6	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td>CP</td></tr><tr><td>5-7</td></tr></table>	CP	5-7	<table border="1" style="display: inline-table; vertical-align: middle;"><tr><td>CP</td></tr><tr><td>2</td></tr></table>	CP	2	intravenous administration
CP									
4-6									
CP									
5-7									
CP									
2									
			in combination with CT						
1 1 1	1 1 1	1	intramuscularly at $17 \pm 0,5$ day-time						
1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1	intramuscularly at $21 \pm 1,0$ evening						

60 ampoules per 2 ml of Erbisol for 24 days.