INSTRUCTION
for medical use of medicinal product
PROTEFLAZID®
(PROTEFLAZIDUM®)

Composition*:*
1 ml of drops contains 1 ml of liquid extract Proteflazid (content of flavonoids not less than 0,32 mg/ml in terms of rutin, content of carbonic acids not less than 0.30 mg/ml in terms of apple acid) from Tufted hair grass (Herba *Deschampsia caespitosa* L.) and bush grass (Herba *Calamagrostis epigeios* L.) (1:1).
Extraction solvent: Ethanol 96%.

Dosage form. Drops.
Main physical and chemical properties: dark greenish liquid with a specific odour.
Pharmacotherapeutic group.
Direct-acting antiviral drugs Code ATX J05A X.

Pharmacological properties
Pharmacodynamics.
Flavonoids which compose the drug are capable of inhibiting replication of DNA- and RNA-viruses both in vitro and in vivo. Inhibitory activity of the drug towards herpes virus, hepatitis, human papillomaviruses, HIV-infection, flu and ARVI has been revealed and proved in pre-clinical and clinical studies.
It has been established that the mechanism of direct antiviral action includes the inhibition of virus specific enzymes – DNA- and RNA-polymerases, thymidine kinase, reverse transcriptase, neuraminidase.
The drug has immunotropic properties. The drug protects mucosae, normalizing the local immunity parameters (lactoferrin, sIgA, lysozyme and C_3 component of the complement).
It has been established that the drug is the inductor of synthesis of endogenous α- and γ-interferons to physiologically active level, increasing organism's non-specific resistance to viral and bacterial infections.

Clinical studies showed that on condition of daily administration of the drug according to the prescribed age-specific dosage variances and dosage regimen the drug does not induce immunotoxic effect and causes no refractoriness (hyporesponsiveness) of immune system and inhibition of the synthesis of α- and γ- interferons which enables a long-tirm use, if necessary.

The drug possesses antioxidant activity, which inhibits free radical processes. Thus it prevents accumulation of lipid peroxidation products, enhances anti-oxidant status of cells, diminishes intoxication, facilitates recovery of a body after infectious disease and adaptation to adverse environmental conditions.
The drug is an apoptosis modulator which intensifies the activity of apoptosis-inducing factors, activatind caspase 9, resulting in quicker elimination of cells affected by viruses and primary prevention of chronic diseases on the background of latent viral infections.
The drug prevents a disease recurrence and prolongs remission period.

Pharmacokineticks.
Active ingredients of the drug are quickly absorbed from gastro-intestinal tract into blood, reaching maximum concentrations within 20 minutes after administration (investigation *in vivo*). Taking into account the present dynamics, half-life excretion from blood plasma takes 2,3 hours. Bioavailability by oral administration makes 80%. Excretion from the body is slow. The level of accumulation of active substances in blood cells is much higher in comparison to blood plasma. Corresponding concentrations of active substances provide prolongation of action of the drug in the body and accumulation in organs and tissues as a result of their release from blood cells. Such pharmacokinetic changes of accumulation and release of active substances by blood cells determine requirement to take the drug twice a day to reach the effective concentrations.

Clinical characteristics
Indications.
Treatment and prophylaxis of recurrences caused by:
- herpes simplex virus type 1 and 2 (*HSV-1, HSV-2*);
- herpes zoster viruses and chicken pox (*HHV-3, type 3*);
- human herpesvirus type 4 (Epstein-Barr virus, EBV), acute and chronic active forms;
- human herpesvirus type 5 (cytomegalovirus, CMV).

Treatment and prophylaxis of flu and other ARVI, including flu caused by viruses of pandemic strains.
In a complex treatment of:
- hepatitis B and C;
- viral, bacterial, fungal infections and their associations (chlamydia, mycoplasma, ureaplasma, etc.);
- HIV-infection and AIDs.

Etiotropic therapy of light and medium forms of cervical dysplasia (CIN1 and CIN2) caused by HPV infection including oncogenic strains.
As a part of a complex therapy of other forms of diseases caused by HPV infection, including oncogenic strains.

Contraindications.
Hypersensitivity to the drug ingredients. Gastroduodenal ulcer.

Interaction with other drugs and other kinds of interactions.
During clinical use it was established that Proteflazid® can be combined with antibiotics and anti-fungal drugs for treatment of viro-bacterial and viro-fungal diseases. No negative manifestations associated with interaction with other drugs have been found.

Administration details.
During the treatment of viral hepatitis in 10-15 % of patients with expressed cytolytic syndrome in 2-4 weeks after the beginning of treatment the increase of activity of aminotransferases, less frequently – of bilirubin level which lasts for 2-4 weeks and does not require withdrawal of the drug can be observed.
Patients with gastro-intestinal disorders and chronic gastroduodenitis in case of recrudescence of gastroduodenitis or esophageal reflux shall take the drug in 1,5-2 hours after meal.

Transient increase in the body temperature to 38 °C does not require the withdrawal of the drug.

In case of increase of the body temperature it is necessary to consult a doctor to exclude other possibilities of that phenomenon.
It is necessary to decrease the concentration of the drug in the solution for application if it causes itching or dryness while being applied topically.
To avoid urinogenital reinfection, simultaneous treatment of a sexual partner is recommended.

Use during pregnancy or breastfeeding.
Pre-clinical studies didn`t reveal any embryotoxic, teratogenic, fetotoxical, mutagenic and oncogenic effects. No special investigations related to such influence of the drug over a human fetus have been conducted, but clinical experience of use of the drug in I-III trimesters of pregnancy and lactation did not reveal any negative influence. A doctor shall decide on advisability of use of the drug during pregnancy or breastfeeding.

Influence on the ability to operate a vehicle or other mechanisms.
No negative influence of Proteflazid over potentially hazardous activities that require special attention and quick reaction has been revealed.

Dosage and Administration
Shake the vial before use.
The drug should be dosed with a dropper. The necessary quantity of the drug should be dropped into water (volume of 1-2 tablespoon) and should be taken in 10-15 minutes before meal.

Age-depending dosage schedule of Proteflazid (ml)

Age (in years)	Dosage (ml) and dosage frequency per day
Since birth to 1 year	1 drop once a day
From 1 to 2 years	1 drop twice a day
From 2 to 4 years	2 drops twice a day
From 4 to 6 years	4 drops twice a day
From 6 to 9 years	9 drops twice a day
From 9 to 12 years	10 drops twice a day
From 12 years and adults	12-15 drops twice a day

Duration of use of Proteflazaid depends on indications and course of disease.

For treatment and prevention of recrudescence of herpetic gingivostomatitis, pharyngotosillitis, chicken pox; for complex treatment of viral, bacterial and mycotic infections and their associations; to avoid viral and bacterial infections which arise in patients with insufficient function of immune system it is recommended to take drug for 1 month.

For treatment of eczema herpeticum and herpetic vesicular dermatitis (together with local application of the solution); herpetic meningitis and encephalitis, herpetic eye lesion; genital herpes; treatment of herpes zoster, acute and chronic forms of Epstein-Barr virus; cytomegalovirus; human papillomavirus (together with local application of the solution) it is recommended to take drug for 3 months without a break.
In case of recurrent infections the treatment should be given 1-2 times per year on the recommendation of a doctor.

Duration of treatment in children is the same as in adults. Doses should be prescribed depending on patient's age, and course of a disease.
Treatment is carried out under a doctor's control.

In a complex therapy of viral hepatitis B and C, HIV-infections and AIDS it is recommended to take the drug for 6-12 months without a break.
Treatment of hepatitis in HIV-infected and AIDS sufferer is carried out before or after antiretroviral therapy.

For treatment of flu and ARVI the drug shall be used for 5-14 days depending on the course of a disease. For prophylaxis the drug should he taken for 2-4 weeks in the dose which makes one-half of the curative dose. During epidemic term of use of the drug may be extended to 6 weeks.

Local use simultaneous with oral intake of the drug:
For treatment of infections of herpes simplex of skin and mucosae, acute forms of herpes zoster, skin papillomatosis solution of the drug shall be applied to the affected area 3-5 times a day.
Exposure period is 10-15 minutes. To prepare solution it is necessary to dissolve 1,5 ml (36-38 drops) in 10 ml of physiological solution of sodium chloride.
Local application shall be continued until signs of skin or mucosal lesion disappear, but not less than for 10 days.
In case of primary or recurent genital herpes, human papillomavirus and viro-bacterial infections of female genital organs vaginal tampons with the drug solution are used. To prepare solution it is necessary to dissolve 3,0 ml (72-75 drops) in 20 ml of physiological solution of sodium chloride. Exposure period of vaginal tampons is 30-40 minutes; manipulation shall be made twice a day.
Duration of local use of vaginal tampons in case of genital herpes is 10 days, in case of human papillomavirus, viral and bacterial infections of female genital organs - 14 days.

Children.
Proteflazid can be used by children since birth.

Overdose.
There is no experience with overdose, however, development of adverse events, especially in gastro-intestinal tract is possible. Symptomatic treatment is recommended.
In case of overdose of Proteflazid, immediately consult a doctor.

Adverse reactions.
Allergic reactions: in patients with increased sensation hypersensitivity reactions are possible.
Sometimes – Rare allergic reactions, including erythematic rash and itching are possible.
Gastrointestinal disorders: very rare: gastrointestinal disorders – pain in epigastric region, nausea, vomit, diarrhea are observed. In patients with chronic gastroduodenitis recrudescence of gastroduodenitis, esophageal reflux is possible.
General disorders: very rare: headache, general weakness, transient increase of body temperature to 38 °C on the 3-10th day of treatment were observed.
Laboratory parameters: By treatment of viral hepatitis in 10-15% of patients with cytolytic syndrome increase of activity of aminotransferases (less frequently - bilirubin level) is observed.
Local reactions: in case of local application burning, itching, dryness may be observed.
Consult a doctor if any adverse reaction occurs.

Shelf-life. 3 years.
Do not use after the end of the shelf-life specified on the package.

Storage conditions.
Store in the original package at the temperature less than 25 °C. Do not freeze!
Formation of a gel-like structure which is destroyed by shaking is possible.
Keep out of reach of children.

Package.
Light-protective glass vials of 30 ml, 50 ml, capped with tamper-evident caps with dropper plugs or tamper-evident and child-resistant closure with dropper plugs in carton package.

Category of prescription.
By prescription.

Manufactured by:
"Scientific & Manufacturing Company "Ecopharm" LTD., 116 Shevchenka Str., Ulashanivka Village, Slavuta District, Khmelnytskyi Region., 30070, Ukraine.

Under Authorisation from:
"Scientific & Manufacturing Company "Ecopharm" LTD., 9-V, Stepana Bandery ave, Kyiv city, 04073, Ukraine.

Date of last revision: