Cerebrolysin®

International Non-Proprietary Name (INN): none

Dosage Form: solution for intramuscular and intravenous injections in ampoules/vials (2, 5, 10 ml)

Structure:
Active substance: 1 ml consists of 215.2 mg of Cerebrolysin concentrate (complex of peptides derived from the pig brain tissue) in aqueous solution. The active fraction of Cerebrolysin is represented by peptides, whose molecular weight does not exceed 10,000 daltons.
Excipients: sodium hydroxide and water for injection.

Description:
Transparent solution of amber color.

Pharmacological classification: nootropics

ATC code: N06BX

Pharmacodynamics:
Cerebrolysin contains low molecular weight biologically active neuropeptides that penetrate the BBB (blood-brain barrier) and directly enter the nerve cells. The drug has an organ-specific multimodal effect on the brain, i.e., provides metabolic regulation, neuroprotection, functional neuromodulation and neurotrophic activity.
Metabolic regulation: Cerebrolysin improves the effectiveness of aerobic energy metabolism of the brain and improves intracellular protein synthesis in both the developing brain and the ageing brain.
Neuroprotection: Cerebrolysin protects neurons from the damaging effects of lactic acidosis, prevents the formation of free radicals, improves survival and prevents the death of neurons under conditions of hypoxia and ischemia and reduces the damaging neurotoxic effect of excitatory amino acids (glutamate).
Neurotrophic activity: Cerebrolysin is the only nootropic peptidergic drug with proven neurotrophic activity similar to that of natural neuronal growth factors (NGF), but manifested under peripheral administration.
Functional neuromodulation: Cerebrolysin has a positive effect on violations of cognitive functions and memorization processes.

Pharmacokinetics:
Complexity of the drug`s composition does not allow for the conducting of the usual pharmacokinetic analysis of individual components, since the Cerebrolysin active fraction consists of a balanced and stable mixture of biologically active oligopeptides with a total polyfunctional action.

Intended uses:
Alzheimer's disease, dementia of various genesis; chronic cerebrovascular insufficiency; ischemic stroke; traumatic brain and spinal cord injuries; mental retardation in children; attention deficit hyperactivity disorder (ADHD) in children; complex therapy of endogenous depression resistant to antidepressants.

Contraindications:
Hypersensitivity to one of the components of the drug, epilepsy and severe renal impairment.
The drug should be prescribed with caution in cases of allergic diathesis, epileptic conditions, including generalized epilepsy, due to the potential for increased seizure frequency.

Dosage and administration:
Intramuscularly (up to 5 ml), intravenously (up to 10 ml), intravenously by slow infusion (10 to 50 ml). **Important: inject slowly over 3 minutes!**
Dosages and duration of treatment depend on the nature and severity of the disease, as well as on the patient's age. It is possible to prescribe single dosages up to 50 ml, but still it is preferable to conduct a course of treatment. The recommended optimal course of treatment is 10-20 dмays of daily injections.

- Acute states (ischemic stroke, traumatic brain injury, complications after neurosurgical operations) – from 10 to 50 ml.
- Residual period (cerebral stroke and traumatic damage of the brain and spinal cord) – from 5 to 50 ml.
- Psycho-organic syndrome and depression – from 5 to 30 ml.
- Alzheimer's disease, dementia of vascular and combined Alzheimer's-vascular genesis – from 5 to 30 ml (1 cycle: 5 days weekly/4 weeks (2-4 cycles per year)).
- In neuropediatric practice – 0.1-0.2 ml / kg.

Treatment courses can be repeated to enhance effectiveness as long as there is an improvement in the patient's condition due to treatment. After the first course the periodicity of dosage administration can be reduced to 2 or 3 times a week.
Dosages of 10 to 50 ml are recommended only through slow intravenous infusions after dilution with the proposed standard solutions for infusion (do not mix with balanced amino acid solutions, vitamins and cardiovascular medicinal products!). The duration of the infusion is 15 to 60 minutes.

Side effects:
The frequency of side reactions was determined in accordance with WHO recommendations: very common (≥1/10); common (from ≥1/100 to <1/10); uncommon (from ≥1/1000 to <1/100); rare (from ≥1/10,000 to <1/1000); very rare, including isolated reports (<1/10,000).

Immune system disorders:
Very rare – hypersensitivity, allergic reactions, skin reactions, neck pain, headache, limb pain, fever, mild back pain, shortness of breath, chills, collapse-like state.

Metabolism and nutrition disorders:
Rare – loss of appetite.

Psychiatric disorders:
Rare – the presumed activation effect may be accompanied by agitation, manifesting as aggressive behavior, confusion, insomnia.

Nervous system disorders:
Rare – rapid administration of the drug may lead to dizziness; very rare – isolated cases of generalized epilepsy and one case of seizure development were associated with the drug Cerebrolysin®.

Cardiovascular system disorders:
Very rare – rapid administration of the drug may lead to palpitations and arrhythmia.

Gastrointestinal disorders:
Very rare – dyspepsia, diarrhea, constipation, nausea, vomiting.

Skin and subcutaneous tissue disorders:
Rare – rapid administration may cause a sensation of heat, sweating, itching.

General disorders and administration site conditions:
Very rare – redness, itching, and burning at the injection site.

One study reported a rare association (from >1/10,000 to <1/1,000) between the use of the drug and hyperventilation, arterial hypertension, hypotension, fatigue, tremor, possible development of depression, apathy, and/or drowsiness, flu-like symptoms (cold, cough, respiratory infections).

Since Cerebrolysin® is mainly used in elderly patients, the above-mentioned disease symptoms are typical for this age group and often occur without the use of the drug.

It should be noted that some adverse effects (agitation, arterial hypertension, hypotension, lethargy, tremor, depression, apathy, dizziness, headache, shortness of breath, diarrhea, nausea) were identified during clinical trials and occurred equally in both Cerebrolysin® and placebo groups.

If any of the side effects listed in the instructions worsen or any other side effects not mentioned in the instructions are observed,

the patient should inform their healthcare provider.

Reporting suspected adverse reactions

It is important to report adverse reactions after the registration of a medicinal product to ensure continuous monitoring of the benefit-risk ratio of the drug. Healthcare professionals are asked to report any adverse reactions observed with the use of the drug through national adverse reaction reporting systems and/or through the company's representative office.

Overdose:

No cases of drug overdose have been reported.

Interaction with other drugs:

Given the pharmacological profile of the drug Cerebrolysin, special attention should be given to possible additive effects when co-prescribing with antidepressants, including MAOIs. In such cases it is recommended to reduce the dosage of antidepressant.

Do not mix Cerebrolysin and balanced amino acid solutions in a single solution for infusions.

Cerebrolysin is incompatible with solutions containing lipids or modifying the pH of the medium (5-8).

Special instructions:

The compatibility of the preparation with the following standard infusion solutions was checked and confirmed (for 24 hours at room temperature and with illumination):

– 0.9% solution of sodium chloride (9 mg NaCl / ml);

– Ringer's solution (Na^+ – 153.98 mmol/l, Ca^{2+} – 2.74 mmol/l, K^+ – 4.02 mmol/l, Cl^- –163.48 mmol/l);

– 5% glucose solution.

It is permissible to use Cerebrolysin simultaneously with vitamins and preparations for cardiac circulation improvement, but these preparations should not be mixed in the same syringe with Cerebrolysin. Use only a clear solution and only once.

Pregnancy and lactation:

The drug may be prescribed with caution in the first trimester of pregnancy and during lactation.

During pregnancy and during breastfeeding Cerebrolysin should only be used after a thorough analysis of the impact of the

positive effect of the treatment and the risk associated with its administration. The results of experimental studies do not give reasons to believe that Cerebrolysin has a teratogenic or a toxic effect on the fetus. However, similar clinical studies have not been conducted.

Influence on the ability to drive vehicles and operate machines:
Clinical trials have shown that Cerebrolysin does not affect the ability to drive vehicles and operate machines.

Terms of release from pharmacy: on prescription.

Storage conditions:
Store at room temperature not exceeding 25°C, do not freeze, protect from light (in the carton). Keep in a safe place out of reach of children.

Shelf life: 5 years. Do not use beyond the expiration date printed on the package.

Country of manufacture: Austria