Nootropil®

International Non-Proprietary Name (INN): Piracetam

Dosage Form: pills

Structure: 1 pill contains:
Active ingredient: piracetam 800 mg or 1200 mg;
Excipients: macrogol 6000, colloidal anhydrous silica (Aerosil R972), magnesium stearate, cross-carmellose sodium, titanium dioxide (E171), macrogol 400, hydroxypropyl methylcellulose.

Description:
Oblong pills with a white or almost white coating and a separating break line on both sides; there is an engraved "N" on one side of the tablet to the right and to left of the break line.

Pharmacological classification: nootropic

ATC code: N06BX03

Pharmacological action: nootropic, antihypoxic, cerebroprotective

Pharmacodynamics:
The active ingredient is Piracetam, a cyclic derivative of gamma-aminobutyric acid (GABA). Improves cognitive processes, such as learning ability, memory, attention and mental performance. Nootropil affects the central nervous system in various ways: it changes the speed of brain excitation spreading, improves metabolic processes in nerve cells, and improves microcirculation by influencing blood rheology without causing vessel-dilating effect.
It improves communication between the cerebral hemispheres and synaptic conduction in neocortical structures, improves mental performance and cerebral blood flow.
Inhibits platelet aggregation and restores the elasticity of the erythrocyte membrane, reduces the red cell adherence.
Provides protective and restorative action in case of impaired brain function caused by hypoxia and intoxication. Piracetam is indicated for treatment of cortical myoclonus both as the monotherapy and as part of the complex therapy.
It reduces the severity and duration of the vestibular nystagmus.

Pharmacokinetics:
Absorption: After ingestion, Piracetam quickly and almost completely absorbs from the gastro-intestinal tract. The bioavailability of Piracetam is close to 100%. After a single dose of 3.2 g the maximum concentration is 84 mcg/ml, after a multiple dose of 3.2 mg 3 times a day the maximum concentration is 115 mcg/ml. Piracetam reaches its maximum concentration in the blood plasma 1 hour after the intake and in the cerebrospinal fluid 5 hours after the intake. The eating lowers the maximum concentration by 17% and increases the time to reach the maximum concentration up to 1.5 hours. For women who take Piracetam at the dose of 2.4 g, the maximum concentration and AUC are 30% higher than for men.
Distribution: Does not bind with blood plasma proteins. Distribution volume is about 0.6 l/kg. Piracetam penetrates through the blood-brain barrier and placental barrier. Animal studies showed that piracetam accumulates selectively in tissues of the cerebral cortex, mainly in the frontal, parietal and occipital lobes, in the cerebellum and in basal nuclei.
Metabolism: Does not metabolize in the body.
Excretion: The half-life is 4-5 hours from the blood plasma and 8.5 hours from the cerebrospinal fluid. The half-life does not depend on the route of administration. 80-100% of Piracetam is excreted in the unchanged form by the kidneys through the glomerular filtration. The total clearance of Piracetam is 80-90

ml/min for healthy volunteers. Half-life is prolonged in case of kidney failure (in case of terminal chronic kidney failure - up to 59 hours). The pharmacokinetics of Piracetam for patients with liver failure does not change.

Intended uses:

- symptomatic treatment of the psycho-organic syndrome (including elderly patients with memory loss, dizziness, reduced ability to concentrate, mood changes, behavioral disorder, gait disorder, as well as patients with Alzheimer's disease and senile Alzheimer-type dementia);
- treatment of consequences of an ischemic stroke, such as speech disorders, emotional disorders, treatment for increasing motor and mental activity;
- treatment of withdrawal syndrome and psycho-organic syndrome in case of chronic alcohol addiction;
- comatose conditions (including the recovery period), including ones after injuries and intoxications of the brain;
- treatment of dizziness and related equilibrium disorders (excluding cases of dizziness of vasomotor and psychogenic origin);
- (as a part of complex therapy) treating of low learning ability in children with psycho-organic syndrome;
- treatment of cortical myoclonia (both in the form of the monotherapy, and as part of the complex therapy);
- sickle cell anemia (as part of the complex therapy).

Contraindications:

- acute cerebrovascular disorder (haemorrhagic stroke);
- terminal stage of kidney failure;
- Huntington's chorea;
- children under 1 year old (in case of solution intake);
- children under 3 years old (in case of pills intake);
- hypersensitivity to the drug ingredients;
- pregnancy and lactation.

With caution: hemostasis disorder, extensive surgical interventions, severe bleeding.

Dosage and administration:

Oral administration (during meals or on an empty stomach with liquid).

Daily doses vary within the range of 30-160 mg/kg of the body weight. Dosage frequency is 2-4 times/day.

Memory and intellectual disorders: 2.4-4.8 g / day, divided into 2-3 administrations.

In case of the chronic psycho-organic syndrome the drug is prescribed at a dose of 2.4-4.8 g/day during the first week, and then the patient is transferred to the maintenance dose of 1.2-2.4 g/day.

When treating consequences of an ischemic stroke Nootropil is prescribed at a dose of 4.8 g/day.

When treating coma and difficulties in perception in people with brain injury, the initial dose is 9-12 g/day, the maintenance dose is 2.4 g/day. The treatment should continue for at least 3 weeks.

When treating abstinence in case of chronic alcohol addiction the dose of the drug reaches 12 g/day during the manifestation of the alcohol withdrawal syndrome. The maintenance dose is 2.4 g/day.

When treating dizziness and related equilibrium disorders the dose is 2.4-4.8 g/day.

In case of cortical myoclonia, the treatment starts with a dose of 7.2 g/day, every 3-4 days the dose is increased by 4.8 g/day until the maximum dose of 24 g/day is reached. The treatment continues throughout the whole period of the disease. Every 6 months attempts should be made to reduce the dose or discontinue the drug gradually reducing the dose by 1.2 g/day every 2 days. In case of lack of efficacy or a slight therapeutic effect, the treatment is discontinued.

In case of sickle cell anemia, the daily preventive dose is 160 mg/kg of the body weight divided into 4 intakes. During the crisis - up to 300 mg/kg intravenous.

Treatment of dyslexia in children (as part of complex therapy): the recommended daily dosage for children from 8 years and adolescents - 3.2 g, divided into 2 administrations.

Special Groups of Patients

Kidney disorder: The dose should be adjusted depending on the amount of creatinine clearance (see the table below).
The creatinine clearance for men can be calculated based on the serum creatinine concentration, according to the following formula:
Creatinine clearance, ml/min = [(140 - age, years) × body weight, kg] / (72 × serum creatinine concentration, mg/dL)
The creatinine clearance for women can be calculated by multiplying the obtained value by a factor of 0.85.

Kidney failure	Creatinine clearance, ml/min	Dose regimen
Missing (norm)	> 80	Usual Dose
Light	50-79	2/3 of the usual dose in 2-3 intakes
Average	30-49	1/3 of the usual dose in 2 intakes
Severe	<30	1/6 of the usual dose in a single intake
End-stage	—	Contraindicated

The dose for elderly patients is adjusted in case of kidney failure. The monitoring of the functional state of the kidneys is necessary in case of the long-term therapy.

Liver disorder: Dose adjustment is not required for patients with the liver failure. For patients with both kidney and liver disorders, the dosing is prescribed according to the scheme (see ‘’Kidney disorder”).

Side effects (rare):
Central nervous system disorders: hyperkinesia (1.72%), nervousness (1.13%), drowsiness (0.96%), depression (0.83%), asthenia (0.23%). These side effects often occur in elderly patients who received the drug at a dose of more than 2.4 g/day. In some cases dizziness, headache, ataxia, balance disorder, and acute condition of epilepsy, insomnia, confusion, agitation, anxiety, hallucinations, increased sexuality are reported.
Metabolism disorders: increase in the body weight (1.29%).
Digestive system disorders: nausea, vomiting, diarrhea, abdominal pains.
Dermatological reactions: dermatitis, itching, rash, swelling.
Blood and lymphatic system: haemorrhagic disorders.
Immune system disorders: anaphylactoid reactions, hypersensitivity.
Hearing disorders: vertigo.

Overdose:
Piracetam is a low toxic drug. When it is taken at a dose of 75 g as a solution for oral administration, dyspeptic disorders such as diarrhea with blood and abdominal pains can occur. No other special symptoms of Piracetam overdose have been reported.
Treatment: immediately after a significant overdose pump the stomach or induce vomiting. Symptomatic therapy, which may include hemodialysis, is indicated. No specific antidote exists. The efficiency of hemodialysis is 50-60%.

Interaction with other drugs:
No interaction of Nootropil with Clonazepam, Phenytoin, Phenobarbital, Sodium Valproate was reported.
Piracetam in high doses (9.6 g/day) increased the effectiveness of Acenocoumarol in patients with venous thrombosis: reports showed greater reduction in the level of aggregation of platelets, in fibrinogen level, in von Willebrand factors, and in blood and plasma viscosity, compared with the case when Acenocoumarol only was prescribed.

The possibility of changing the pharmacodynamics of Piracetam under the influence of other drugs is low, because 90% of its dose is excreted in the urine in the unchanged form.
In vitro Piracetam at concentrations of 142, 426 and 1422 μg/ml does not inhibit the activity of the isoenzymes CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1 and 4A9/11. At a concentration of 1422 μg/ml, slight inhibition of the activity of the isoenzymes CYP2A6 (21%) and 3A4/5 (11%) is reported. However, the level of the inhibition constant (Ki) of these two isoenzymes is sufficient in case there is an exceeding of 1422 μg/ml. Therefore, metabolic interaction with other drugs is unlikely.
When Piracetam is taken at a dose of 20 mg/day, there is no changing of the maximum concentrations in the blood plasma and of the nature of the pharmacokinetic curve of antispasmatic medications (Carbamazepine, Phenytoin, Phenobarbital, valproic acid) in patients with epilepsy receiving constant doses of these medications. When Piracetam was taken at a dose of 1.6 g with alcohol, the concentrations of Piracetam and ethanol in the serum remained unchanged.

Pregnancy and lactation:
Adequate and strictly controlled studies of the safety of the use of Nootropil during pregnancy have not been conducted. In experimental studies on animals, no damaging effects on the embryo and its development (including the postnatal period) and no changes in the course of pregnancy and childbirth have been identified.
The drug should not be prescribed during pregnancy, except cases of emergency. Piracetam penetrates through the placental barrier and is excreted in breast milk. The concentration of Piracetam in newborns reaches 70-90% of its concentration in the blood of the mother. If taking of the drug is required during lactation, breastfeeding should be discontinued.

Influence on the ability to drive vehicles and operate mechanisms:
Taking into account possible undesirable effects, the patient should be careful when operating mechanisms and driving vehicles.

Special precaution:
Nootropil should be taken no later than 5 pm to prevent sleep disturbances.
Due to the antiaggregant effect (see "Pharmacodynamics"), Piracetam should be prescribed with caution to patients with severe haemorrhagic disorders, risk of bleeding (for example, in case of the stomach ulcer), hemostasis disorders, haemorrhagic cerebrovascular disorders in anamnesis, to patients with surgical interference, including dental interference, to patients receiving anticoagulants and antiplatelet agents, including low-doses of acetylsalicylic acid.
When treating patients with cortical myoclonia, abrupt discontinuation of the therapy should be avoided. This can cause episode relapse.
In the treatment of sickle cell anemia, a dose of less than 160 mg/kg or an irregular administration of the drug may cause disease exacerbation.
In case of a long-term therapy of elderly patients, regular monitoring of kidney function indicators is recommended; if necessary, the dose is adjusted depending on the results of the creatinine clearance study.
Nootropil penetrates through the filtration membranes of hemodialysis apparatus.
When treating patients on the hyposodium diet, it should be noted that Piracetam pills at a dose of 24 g contain 46 mg of sodium.

Terms of release from pharmacy: on prescription

Storage conditions: store in a dry place at temperatures no higher than 25°C. Keep out of reach of children.

Shelf life: 4 years. Do not use beyond the expiration date.

Country of manufacture: Belgium