G1-1228-22-F

Nootropil®

PHARMACOLOGY

NOOTROPIL (piracetam) is a "nootrope", that is to say it is a psychotropic agent which acts directly on the brain to improve the efficacy of the telencephalon.
NOOTROPIL can act on the Central Nervous System in a variety of ways. It will modify neurotransmission within the brain, and can help to improve the metabolic environment essential for good neuronal function. It is also a haemorrheological agent and can improve microcirculation without producing vasodilation.
When given as acute or long term treatment for patients suffering from a functional CNS deficit, it will heighten alertness and increase cognitive function. These changes are seen as a significant increase in the alpha and beta activity, with a reduction in delta activity, on an EEG trace.
NOOTROPIL will protect and restore cognitive functional capacity after cerebral trauma such as hypoxia or intoxication, and after electroshock therapy.
NOOTROPIL may be given alone, or together with other drugs when treating cortical myoclonia. NOOTROPIL will reduce the duration of vestibular nystagmus.
NOOTROPIL will inhibit the increased aggregation of activated platelets and, in conditions where there is abnormal rigidity of the red blood cell, it can restore deformability and the ability to pass through the microvasculature.

PHARMACOKINETICS

When given by mouth, in either solute or tablet form, NOOTROPIL is rapidly and almost totally absorbed in the gut. Bioavailability is almost 100%.
When given as a single 2 g dose, the peak blood level of 40 to 60 µg/ml is attained after 30 minutes. In the cerebrospinal fluid the peak concentration is achieved at 2 to 8 hours post-dosage.
The apparent volume of distribution is in the region of 0.6 l/kg. Plasma half-life is 4 to 5 hours, while the half-life in the cerebrospinal fluid is 6 to 8 hours.
The half-life is increased in cases of renal insufficiency.
NOOTROPIL does not bind to plasma proteins and is eliminated unchanged principally via the kidney. Renal excretion is almost complete, i.e. over 95%, after 30 hours.
Renal clearance of NOOTROPIL in healthy volunteers is 86 ml/minute.
NOOTROPIL will diffuse into all types of tissue and can cross both the blood-brain barrier and the placenta, as well as the membranes employed in renal dialysis.
NOOTROPIL is active in its unchanged form and is not metabolised by any of the animal species tested.
NOOTROPIL is concentrated in the cerebral cortex, in the frontal, parietal and occipital lobes, in the cerebellum and in the basal ganglia.

INDICATIONS

1. NOOTROPIL is proposed for symptomatic improvement of memory and intellectual disorders in the frame of a pathology, without diagnosis of dementia.
2. NOOTROPIL can reduce cortical myoclonias in some patients. In order to assess the patient's response to NOOTROPIL, a test treatment may therefore be started for a limited period of time.
3. Studies have shown some improvement in children with learning difficulties associated with the written word, particularly with textual understanding which cannot be explained by intellectual backwardness, inadequate education or by the family environment. The administration of NOOTROPIL does not replace other measures also well adapted to correct these learning difficulties, such as remedial teaching.

DOSAGE AND ADMINISTRATION

- Memory or intellectual disorders:
  Loading treatment: 4.8 g per day in several intakes during the first weeks of the treatment, followed by a maintenance treatment of 2.4 g per day in two or three intakes, possibly lowered to 1.2 g per day.
- In the treatment of cortical myoclonias, the initial dosage is 24 g of NOOTROPIL per 24 hours for 3 days.
  In case of a weak or no response on the 3rd day, the administration of 24 g of NOOTROPIL will be continued until the 7th day. If there is still an insufficient or no response, treatment will be discontinued on the 7th day. As soon as the the 24 g dose becomes active, it will be decreased by 1.2 g every other day until myoclonus appears again. This method enables to determine the mean active dose. The daily dose of NOOTROPIL will be given in 2 or 3 intakes. Treatment with other anti-myoclonic drugs will be maintained using the same dosage. Thereafter, depending on the clinical benefit obtained, the dosage of the other anti-myoclonic drugs will be reduced, if possible. The initiated treatment with NOOTROPIL will be maintained as long as the initial cerebral pathology persists. A decrease or discontinuation of drug therapy will nevertheless be made tentatively every 6 months. Treatment will be discontinued by reducing the dose of NOOTROPIL by 1.2 g every other day, in order to avoid a sudden relapse of the disease.
  The injectable form is to be used if oral route is not possible. Intravenous injection should be performed over several minutes; the infusion should be administered continuously, at the recommended daily dose, over 24 hour period.
- In the treatment of 8 to 13 year-old children with learning difficulties NOOTROPIL is given at a total dose of 3.3 g daily. This is administered either as 8 ml of a 20% solution or 5 ml of a 33% solution twice a day i.e. before breakfast and before the evening meal.
  The medication may be more easily accepted if given in fruit juice, or in some other drink.
  Treatment should be continued throughout the school year. The efficacy of a longer period of treatment has not yet been investigated.

CONTRA-INDICATIONS

Hypersensitivity to piracetam or other pyrrolidone derivates or any of the excipients.
Piracetam is contra-indicated in patients with cerebral haemorrhage.
Piracetam is contra-indicated in End Stage Renal Disease patients.
NOOTROPIL granules contain aspartam sweetener and should not be used by patients having phenylketonuria, especially children, as aspartam contains phenylalanine.

UNDESIRABLE EFFECTS

Undesirable effects that may be reported during treatment with NOOTROPIL are: anxiety, sleep disturbances, headache, vertigo, hyperkinesia, ataxia, hallucination and confusion.
The incidence of these during clinical trials was 5% or less, and they were more often noted in the older patients taking more than 2.4 g daily. In the majority of cases a dose reduction sufficed to make these symptoms disappear.
Some patients may complain of fatigue or drowsiness.
Gastro-intestinal problems such as nausea, vomiting, diarrhoea and stomach ache have also been reported, but their incidence during clinical trials was 2% or less.
Occasionally tremor and sexual stimulation have also been reported.
Allergic reactions (pruritus, rash, urticaria, angioneurotic oedema) have been reported.
Rare cases of injection site pain, thrombophlebitis, pyrexia, or hypotension have been reported after intravenous administration.
Pre-existing epilepsy worsening may occur.

PRECAUTIONS

Due to the effect of piracetam on platelet aggregation, caution is recommended in patients with underlying disorders of haemostatis, major surgery or severe haemorrhage.
As the principal route of elimination for NOOTROPIL (piracetam) is via the kidney, special care must be taken when treating patients known to suffer from renal insufficiency.
Monitoring of renal function is recommended in such cases. The increase in half-life is directly related to the decrease in renal function and creatinine clearance. This is also true for the older patient in whom creatinine clearance is dependent on age.

For this reason, the dosage will be adjusted according to the table below:

Group	Creatinine clearance (ml/min)	Posology and frequency
Normal	> 80	usual dose, 2 to 4 sub-doses
Mild	50-79	2/3 usual daily dose, 2 or 3 sub-doses
Moderate	30-49	1/3 usual daily dose, 2 sub-doses
Severe	< 30	1/6 usual daily dose, 1 single intake
End-Stage Renal Disease	–	contra-indicated

Abrupt discontinuation of treatment should be avoided in myoclonic patients as this may induce sudden relapse or withdrawal seizures.

INCOMPATIBILITY

None reported to date.

PREGNANCY AND BREAST FEEDING

NOOTROPIL should not be prescribed during pregnancy or when breast feeding, except under exceptional circumstances.
NOOTROPIL is able to cross the placenta.

DRUG INTERACTIONS

Only one case of interaction has been reported, where NOOTROPIL and thyroid extract (T3 & T4) were given together and confusion, irritability and sleep disturbances were later observed.
In a published single-blind study on patients with severe recurrent venous thrombosis, piracetam 9.6 g/d did not modify the doses of acenocoumarol necessary to reach INR 2.5 to 3.5, but compared with the effects of acenocoumarol alone, the addition of piracetam 9.6 g/d significantly decreased platelet aggregation, β-thromboglobulin release, levels of fibrinogen and von Willebrand's factors (VIII: C; VIII: vW: Ag; VIII: vW: RCo) and whole blood and plasma viscosity.
The drug interaction potetial resulting in changes of piracetam pharmacokinetics is expected to be low because approximately 90% of the dose of piracetam is excreted in the urine as unchanged drug.
In vitro, piracetam does not inhibit the major human liver cytochrome P450 isoforms (CYP 1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, 3A4/5 and 4A9/11) at concentrations of 142,426 and 1422 µg/ml. Therefore, metabolic interaction of piracetam with other drugs is unlikely
A 20 g daily dose of piracetam over 4 weeks did not modify the peak and trough serum levels of antiepileptic drugs (carbamazepine, phenytoin, phenobarbitone, valproate) in epileptic patients who were receiving stable doses.
Concomitant administration of alcohol had no effect on piracetam serum levels and alcohol levels were not modified by a 1.6 g oral dose of piracetam.
No other drug interactions have been described.

OVERDOSAGE

- Symptoms

One case of bloody diarrhoea with abdominal pain, associated with the oral intake of 75 g piracetam daily, was most probably related to the extreme high dose of sorbitol contained in the used formulation.
No other case was reported that would point to additional adverse events specifically related to overdose.

- Management of overdose

In acute, significant overdosage, the stomach may be emptied by gastric lavage or by induction of emesis. There is no specific antidote for overdose with piracetam. Treatment for an overdose will be symptomatic treatment and may include hemodialysis. The extraction efficiency of the dialyser is 50 to 60% for piracetam.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Given the adverse events observed with the drug, an influence on driving and using machines is possible and should be taken into account.

STORAGE

All dosage forms of the product should be stored at room temperature (15°C-25°C).

STABILITY

The expiry date should be checked. This is indicated on the packing after the word "Exp.:", the four figures given indicate the month, as from the first day, and the year after which the product will be time-expired.

HOW SUPPLIED

Oral preparations:
- 60 Capsules of piracetam 400 mg
- 30 Film-coated tablets of piracetam 800 mg
- 20 Film-coated tablets of piracetam 1200 mg
- 20 Granule sachets of piracetam 1200 mg
- 200 ml Bottle of 20% solution (1 ml = 200 mg piracetam)
- 125 ml Bottle of 33% solution (1 ml = 333 mg piracetam)

Preparations for injections:
- 12 Ampoules of piracetam 1 g/5 ml
- 4 Ampoules of piracetam 3 g/15 ml
- Vial for intravenous infusion of piracetam 12 g/60 ml.

Should any complaint arise, please mention the batch control number indicated on the package.

Manufacturer infusion solution:
UCB PHARMA S.P.A.
PIANEZZA (TO) · ITALY

Manufacturer other forms:
UCB S.A. PHARMA SECTOR
BRAINE-L'ALLEUD · BELGIUM

G1-1228-22-F

(ان هـــذا الـــدواء)

- الدواء مستحضر يؤثر على صحتك واستهلاكه خلافا للتعليمات يعرضك للخطر
- اتبع بدقه وصفة الطبيب وطريقة الاستعمال المنصوص عليها وتعليمات الصـــيدلانى الـذى صرفها لك .
- فالطبيب والصيدلانى هما الخبيران بالدواء وبنفعه وضرره .
- لاتقطع مـدة العـلاج المحـدده لك من تلقـاء نفسـك .
- لاتكـرر صـرف الـدواء بـدون وصـفه طـبيبه .

لاتترك الادويه فى متناول ايدى الاطفال

مجلس وزراء الصحة العرب
واتحاد الصيادلة العرب

THIS IS A MEDICAMENT

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The Doctor and the Pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your Doctor.

Keep medicament out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists