Front

PIRACETAM

NEUROCETAM ™

800 mg Tablet

PSYCHOANALEPTIC

PRODUCT DESCRIPTION:
White, Oblong shaped, film coated tablets, with break line on one surface

FORMULATION/COMPOSITION:
Each film-coated tablet contains:
Piracetam ..... 800 mg

PHARMACODYNAMICS/PHARMACOKINETICS:
Pharmacodynamics:
Piracetam mode of action in cortical myoclonus is as yet unknown.
Pharmacodynamic effects
Piracetam exerts its hemorheological effects on the platelets, red blood cells, and vessel walls by increasing erythrocyte deformability and by decreasing platelet aggregation, erythrocyte adhesion to vessel walls and capillary vasospasm.
- Effects on the red blood cells:
In patients with sickle cell anaemia, Piracetam improves the deformability of the erythrocyte membrane, decreases blood viscosity, and prevents rouleaux formation.
- Effects on platelets:
In open studies in healthy volunteers and in patients with Raynaud's phenomenon, increasing doses of piracetam up to 12 g was associated with a dose-dependent reduction in platelet functions compared with pre-treatment values (tests of aggregation induced by ADP, collagen, epinephrine and ßTG release), without significant change in platelet count. In these studies, piracetam prolonged bleeding time.
- Effects on blood vessels:
In animal studies, piracetam inhibited vasospasm and counteracted the effects of various spasmogenic agents. It lacked any vasodilatory action and did not induce "steal "phenomenon, nor low or no reflow, nor hypotensive effects.
In healthy volunteers, piracetam reduced the adhesion of RBCs to vascular endothelium and possessed also a direct stimulant effect on prostacyclin synthesis in healthy endothelium.
-Effects on coagulation factors:
In healthy volunteers, compared with pre-treatment values, piracetam up to 9.6 g reduced plasma levels of fibrinogen and von Will brand's factors (VIII : C; VIII R : AG; VIII R : vW) by 30 to 40 %, and increased bleeding time.
In patients with both primary and secondary Raynaud phenomenon, compared with pre-treatment values, piracetam 8 g/d during 6 months reduced plasma levels of fibrinogen and von Will brand's factors (VIII : C; VIII R : AG; VIII R : vW (RCF)) by 30 to 40 %, reduced plasma viscosity, and increased bleeding time.

Pharmacokinetics:
Absorption: Piracetam is rapidly and almost completely absorbed. Peak plasma levels are reached within 1.5 hours after administration. The extent of oral bioavailability, assessed from the Area under Curve (AUC), is close to 100% for capsules, tablets and solution. Peak levels and AUC are proportional to the dose given.
Distribution: The volume of distribution of piracetam is 0.7 L/kg. Piracetam crosses the blood-brain and the placental barrier and diffuses across membranes used in renal dialysis.
Biotransformation: Up to now, no metabolite of piracetam has been found.
Elimination; Piracetam is excreted almost completely in urine and the fraction of the dose excreted in urine is independent of the dose given. Excretion half-life values are consistent with those calculated from plasma / blood data. The plasma half-life is 5.0 hours, in young adult men Clearance of the compound is dependent on the renal creatinine clearance and would be expected to diminish with renal insufficiency.

INDICATIONS:
Piracetam is indicated in adult patients suffering from myoclonus of cortical origin, irrespective of aetiology, and should be used in combination with other anti-myoclonic therapies.

DOSAGE AND MODEL ROUTE OF ADMINISTRATION:
Posology
The daily dosage should begin at 7.2 g increasing by 4.8 g every three to four days up to a maximum of 24 g, divided in two or three doses. Treatment with other anti-myoclonic medicinal products should be maintained at the same dosage. Depending on the clinical benefit obtained, the dosage of other such medicinal products should be reduced, if possible.
Once started, treatment with piracetam should be continued for as long as the original cerebral disease persists. In patients with an acute episode, spontaneous evolution may occur over time and an attempt should be made every 6 months to decrease or discontinue the medicinal treatment. This should be done by reducing the dose of piracetam by 1.2 g every two days (every three or four days in the case of a Lance and Adams syndrome, in order to prevent the possibility of sudden relapse or withdrawal seizures).
Elderly
Adjustment of the dose is recommended in elderly patients with compromised renal function. For long term treatment in the elderly, regular evaluation of the creatinine clearance is required to allow dosage adaptation if needed.
Patients with renal impairment
The daily dose must be individualized according to renal function. Refer to the following table and adjust the dose as indicated. To use this dosing table, an estimate of the patient's creatinine clearance (CLcr) in ml/min is needed. The CLcr in ml/min may be estimated from serum creatinine (mg/dl) determination using the following formula:

$$\text{Clcr} = \frac{[140\text{-age (years)}] \times \text{weight (kg)} \times 0.85 \text{ for women}}{72 \times \text{serum creatinine (mg/dl)}}$$

Group	Creatinine Clearance (ml/min)	Posology and frequency
Normal	> 80	usual daily dose, divided in 2 to 4 doses
Mild	50-79	2/3 usual daily dose, divided in 2 or 3 doses
Moderate	30-49	1/3 usual daily dose, divided in 2 doses
Severe	< 30	1/6 usual daily dose, 1 single intake
End-stage renal disease	--	contraindicated

Patients with hepatic impairment
No dose adjustment is needed in patients with solely hepatic impairment. In patients with hepatic impairment and renal impairment, adjustment of dose is recommended (see 'Dosage adjustment in patients with renal impairment' above).
Method of administration
Piracetam should be administered orally, and may be taken with or without food. The tablet(s) should be swallowed with liquid. It is recommended to take the daily dose in two to four sub-doses.

CONTRAINDICATIONS &PRECAUTION(S), WARNING(S):
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 or other pyrrolidone derivatives.
Piracetam is contra-indicated in patients with severe renal impairment (renal creatinine clearance of less than 20 ml per minute). It is also contraindicated in patients with cerebral haemorrhage and in patients suffering from Huntington's Chorea.

PRECAUTIONS & WARNINGS:
Effects on platelet aggregation
Due to the effect of piracetam on platelet aggregation (see section 5.1), caution is recommended in patients with severe haemorrhage, patients at risk of bleeding such as gastrointestinal ulcer, patients with underlying disorders of hemostasis, patients with history of hemorrhagic cerebro-vascular accident (CVA), patients undergoing major surgery including dental surgery, and patients using anticoagulants or platelet antiaggregant drugs including low dose acetylsalicylic acid.
Renal insufficiency
Piracetam is eliminated via the kidneys and care should thus be taken in cases of renal insufficiency
Elderly
For long-term treatment in the elderly, regular evaluation of the creatinine clearance is required to allow dosage adaptation if needed.
Discontinuation

Size: 170 x 240 mm

Abrupt discontinuation of treatment should be avoided as this may induce myoclonic or generalized seizures in some myoclonic patients.
Warnings related to the excipients
This product contains about 2 mmol (or about 46 mg) sodium per 24 g piracetam. To be taken into consideration by patients on a controlled sodium diet.

PREGNANCY AND LACTATION:
Pregnancy: There are no adequate data from the use of piracetam in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal / foetal development, parturition or post-natal development.
Piracetam crosses the placental barrier. Drug levels in the newborn are approximately 70% to 90% of maternal levels. Piracetam should not be used during pregnancy unless clearly necessary, when benefit exceeds the risks and the clinical condition of the pregnant mother requires treatment with piracetam.
Breast-feeding: Piracetam is excreted in human breast milk. Therefore, piracetam should not be used during breastfeeding or breastfeeding should be discontinued, while receiving treatment with piracetam. A decision must be made whether to discontinue breast-feeding or to discontinue piracetam therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

INTERACTIONS:
Pharmacokinetics interactions
The drug interaction potential 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 human liver cytochrome P450 isoforms CYP 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1 and 4A9/11 at concentrations of 142, 426 and 1422 µg/ml.
At 1422 µg/ml, minor inhibitory effects on CYP 2A6 (21%) and 3A4/5 (11%) were observed. However, the Ki values for inhibition of these two CYP isoforms are likely to be well in excess of 1422 µg/ml. Therefore, metabolic interaction of piracetam with other drugs is unlikely.
Thyroid hormones
Confusion, irritability and sleep disorder have been reported during concomitant treatment with thyroid extract (T3 + T4).
Acenocoumarol
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.
Antiepileptic drugs
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, and valproate) in epileptic patients who were receiving stable doses.
Alcohol
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.

ADVERSE EFFECTS:
a. Summary of safety profile
Double-blind placebo-controlled clinical or pharmaco Clinical trials, of which quantified safety data are available (extracted from the UCB Documentation Data Bank on June 1997), included more than 3000 subjects receiving piracetam, regardless of indication, dosage form, daily dosage or population characteristics.
b. Tabulated list of adverse reactions
Undesirable effects reported in clinical studies and from post-marketing experience are listed in the following table per System Organ Class and per frequency. The frequency is defined as follows: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000).
Data from post-marketing experience are insufficient to support an estimate of their incidence in the population to be treated.
Blood and lymphatic system disorders
Not known: hemorrhagic disorder
Immune system disorders:
Not known: anaphylactoid reaction, hypersensitivity
Psychiatric disorders:
Common: nervousness
Uncommon: depression
Not known: agitation, anxiety, confusion, hallucination
Nervous system disorders:
Common: hyperkinesia
Uncommon: somnolence
Not known: ataxia, balance impaired, epilepsy aggravated, headache, insomnia,
Ear and labyrinth disorders:
Not known: vertigo
Gastrointestinal disorders:
Not known: abdominal pain, abdominal pain upper, diarrhoea, nausea, vomiting
Skin and subcutaneous tissue disorders:
Not known: angioneurotic oedema, dermatitis, pruritus, urticaria
General disorders and administration site conditions:
Uncommon: asthenia
Investigations
Common: weight increased

OVERDOSAGE AND TREATMENT:
Symptoms: No additional adverse events specifically related to overdose have been reported with piracetam.
The highest reported overdose with piracetam was oral intake of 75 g. 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.
Management of overdose: In acute, significant over dosage, 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.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

DOSAGE FORMS AND PACKAGING AVAILABLE:
Piracetam Tablets 800 mg (Neurocetam) is packed in Alu-Orange PVC Blister pack of 10's (Box of 30's)

INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE):
Not Applicable

NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:
Marketing Authorization Holder
Brown & Burk Philippines Inc
U-501, 5/F., SEDCCO 1 Bldg., 120 Rada cor.,
Legaspi Sts., Legaspi Village, Makati City, Philippines

NAME AND ADDRESS OF MANUFACTURER:
MICRO LABS LIMITED
92, SIPCOT HOSUR-635 126,
TAMIL NADU, INDIA

CAUTION STATEMENT:
FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

ADR REPORTING STATEMENT:
"FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA:
www.fda.gov.ph
Seek medical attention immediately at the first sigh of Adverse Drug Reaction.

REGISTRATION NUMBER:
DR No. : XY34886

DATE OF FIRST AUTHORIZATION:
17 June 2010

DATE OF REVISION OF PACKAGE INSERT:
Feb. 2017

EXG-ML01I-0319/C

MICRO LABS LIMITED, BANGALORE, INDIA							
1	Product Name	Neurocetam				Colours Used	
2	Strength	800 mg				BLACK	
3	Component	Leaflet					
4	Category	Export - Philippines					
5	Dimension	170 x 240 mm					
6	Artwork Code	EXG-ML01I-0319/B					
7	Pharma Code	N/A					
8	Reason for Change	Size & text					

	Prepared by (DTP)	Checked by (PD)	Approved by			
			Head CQA	Head Production/ Packing (Site)	Head QC (Site)	Head QA (Site)
Sign	Kantharaju L.					
Date	06-06-2020					