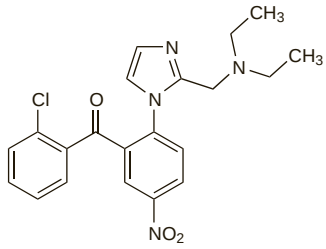
Nizofenone *(rINN)*

Nizofenona; Nizofénone; Nizofenonum; Y-9179. 2′-Chloro-2-[2-[(diethylamino)methyl]imidazol-1-yl]-5-nitrobenzophenone.

Низофенон

$C_{21}H_{21}ClN_4O_3$ = 412.9.
CAS — 54533-85-6.
ATC — N06BX10.
ATC Vet — QN06BX10.



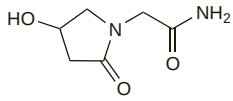
Profile
Nizofenone has been investigated as a nootropic and cerebral vasodilator. It has been used parenterally as the fumarate.

Oxiracetam *(BAN, rINN)*

CGP-21690E; CT-848; ISF-2522; Oksirasetaami; Oxiracétam; Oxiracetamum; Oxracetam. 4-Hydroxy-2-oxo-1-pyrrolidineacetamide.

Оксирацетам

$C_6H_{10}N_2O_3$ = 158.2.
CAS — 62613-82-5.
ATC — N06BX07.
ATC Vet — QN06BX07.



Profile
Oxiracetam has been used as a nootropic in organic brain syndromes and senile dementia.

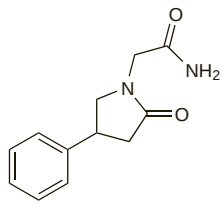
Dementia. Clinical benefit has been reported in patients with dementia (p.362) given oxiracetam,[1] but in the USA it was withdrawn from phase II clinical studies in patients with Alzheimer's disease due to lack of efficacy.[2]

1. Maina G, *et al*. Oxiracetam in the treatment of primary degenerative and multi-infarct dementia: a double-blind, placebo-controlled study. *Neuropsychobiology* 1990; **21**: 141–5.
2. Parnetti L. Clinical pharmacokinetics of drugs for Alzheimer's disease. *Clin Pharmacokinet* 1995; **29:** 110–29.

4-Phenylpiracetam ⊗

BRN-5030440; Carphedon; Karfedon. 2-Oxo-4-phenyl-1-pyrrolidineacetamide.

$C_{12}H_{14}N_2O_2$ = 218.3.
CAS — 77472-70-9.



Profile
4-Phenylpiracetam is a nootropic and has been used in the management of various cerebrovascular disorders. It has also been abused in sport.

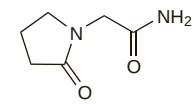
Preparations
Proprietary Preparations (details are given in Part 3)
Rus.: Phenotropil (Фенотропил).

Piracetam *(BAN, USAN, rINN)*

CI-871; Piracétam; Piracetamas; Piracetamum; Pirasetaami; Pirasetam; Pyrrolidone Acetamide; UCB-6215. 2-(2-Oxopyrrolidin-1-yl)acetamide.

Пирацетам

$C_6H_{10}N_2O_2$ = 142.2.
CAS — 7491-74-9.
ATC — N06BX03.
ATC Vet — QN06BX03.



Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Piracetam). A white or almost white powder. It exhibits polymorphism. Freely soluble in water; soluble in alcohol. Protect from light.

Adverse Effects and Precautions
Piracetam is reported to produce insomnia or somnolence, weight gain, hyperkinesia, nervousness, and depression. Other reported adverse effects include gastrointestinal disorders such as abdominal pain, diarrhoea, nausea and vomiting, hypersensitivity reactions, ataxia, vertigo, confusion, hallucinations, angioedema, and rashes. Piracetam should not be given to patients with hepatic impairment or severe renal impairment; dosage reduction is recommended for those with mild to moderate renal impairment. Therapy with piracetam should not be withdrawn abruptly in myoclonic patients due to the risk of inducing seizures. When used to treat cortical myoclonus, piracetam is contra-indicated in patients with cerebral haemorrhage, and should be used with caution after major surgery and in those with haemostatic disorders or severe haemorrhage.

Interactions
Anticoagulants. For reference to the effect of piracetam on *warfarin* therapy, see p.1431.

Pharmacokinetics
Piracetam is rapidly and extensively absorbed from the gastrointestinal tract; peak plasma concentrations are reached within 1.5 hours after oral doses. The plasma half-life is reported to be 5 hours and it crosses the blood-brain barrier. Piracetam is excreted almost completely in the urine. It crosses the placenta and is distributed into breast milk.

Uses and Administration
Piracetam acts on the CNS and has been described as a nootropic; it is said to protect the cerebral cortex against hypoxia. It is also reported to inhibit platelet aggregation and reduce blood viscosity at high doses. Piracetam is used as an adjunct in the treatment of myoclonus of cortical origin, and has also been used in dementia (see also below). Other disorders or states in which it has been tried (on the basis of a supposed 'cerebrocortical insufficiency' responsive to piracetam) include alcoholism, vertigo, cerebrovascular accidents, dyslexia, behavioural disorders in children, and after trauma or surgery.

In cortical myoclonus, piracetam is given in oral doses of 7.2 g daily increasing by 4.8 g daily every 3 or 4 days up to a maximum of 20 g daily. It is given in 2 or 3 divided doses. Once the optimal dose of piracetam has been established, attempts should be made to reduce the dose of other drugs. For dosage in renal impairment see below.

Piracetam has been given for various other disorders in a usual oral dose of up to 2.4 g daily in 2 or 3 divided doses; higher doses of up to 4.8 g daily have been used in severe cases. In severe disorders it has also been given by intramuscular or intravenous injection.

◊ General references.
1. Winblad B. Piracetam: a review of pharmacological properties and clinical uses. *CNS Drug Rev* 2005; **11:** 169–82.

Administration in renal impairment. Dosage should be reduced in patients with mild to moderate renal impairment according to creatinine clearance (CC):
- CC between 50 and 79 mL/minute: two-thirds of the usual dose, given in 2 or 3 divided doses
- CC between 30 and 49 mL/minute: one-third of the usual dose, given in 2 divided doses
- CC between 20 and 29 mL/minute: one-sixth of the usual dose, given as a single dose
- CC less than 20 mL/minute: contra-indicated

Dementia. Although piracetam is used in some countries in the management of cognitive impairment and dementia (p.362), a systematic review[1] concluded that the evidence from the published literature did not support this use.

1. Flicker L, Grimley Evans J. Piracetam for dementia or cognitive impairment. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 14/02/06).

Myoclonus. A review[1] of 62 case reports, 3 open studies, and 2 double-blind studies concluded that piracetam is beneficial in the treatment of disabling myoclonus (p.470), either as adjunctive treatment or as monotherapy. Similar conclusions were made in another review[2] in which experience of 12 patients with progressive myoclonus epilepsy, 8 of whom benefited from piracetam in doses of up to 45 g daily without significant adverse effects, was described.

1. Van Vleymen B, Van Zandijcke M. Piracetam in the treatment of myoclonus: an overview. *Acta Neurol Belg* 1996; **96:** 270–80.
2. Genton P, *et al*. Piracetam in the treatment of cortical myoclonus. *Pharmacopsychiatry* 1999; **32** (suppl): 49–53.

Stroke. Piracetam did not influence the outcome if given within 12 hours of the onset of acute ischaemic stroke in a multicentre, randomised, double-blind study,[1] although post hoc analyses suggested that it might confer benefit when given within 7 hours of onset, particularly in patients with stroke of moderate to severe degree. Further analyses of the same data concluded that piracetam did not produce significant adverse effects when given in high doses to patients with acute stroke,[2] and significantly more patients had recovered from aphasia on piracetam than placebo.[3] The results of two further randomised, double-blind, placebo-controlled studies supporting the role of piracetam as an adjunct to intensive speech therapy in improving aphasia following stroke were also reported.[3] In contrast, a systematic review including the first study considered that the trend towards an increased risk of early death in patients allocated to piracetam was of concern, and concluded that the data did not support routine use of piracetam in acute ischaemic stroke.[4]

1. De Deyn PP, *et al*. Treatment of acute and ischemic stroke with piracetam. *Stroke* 1997; **28:** 2347–52.
2. De Reuck J, Van Vleymen B. The clinical safety of high-dose piracetam—its use in the treatment of acute stroke. *Pharmacopsychiatry* 1999; **32** (suppl): 33–7.
3. Huber W. The role of piracetam in the treatment of acute and chronic aphasia. *Pharmacopsychiatry* 1999; **32** (suppl): 38–43.
4. Ricci S, *et al*. Piracetam for acute ischaemic stroke. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 23/05/08).

Vertigo. Piracetam has been reported to be of benefit in patients with vertigo (p.565) of both central or peripheral origin.[1]

1. Oosterveld WJ. The effectiveness of piracetam in vertigo. *Pharmacopsychiatry* 1999; **32** (suppl): 54–60.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Noostan; ***Austria:*** Cerebryl; Nootropil; Novocephal; Pirabene; ***Belg.:*** Braintop; Docpirace; Geratam; Noodis; Nootropil; Piracemed; Piracetop; ***Braz.:*** Cintilan; Nootrofic†; Nootron; Nootropil; ***Chile:*** Nootropyl; ***Cz.:*** Cerebryl†; Geratam; Kalicor; Nootropil; Oikamid; Pirabene; ***Fin.:*** Nootropil; ***Fr.:*** Axonyl†; Gabacet; Geram†; Nootropyl; ***Ger.:*** Avigilen; Cerebroforte†; Cerepar N; Cuxabrain†; Memo-Puren†; Nootrop; Normabrain; Piracebral; Piracetrop; Sinapsan; ***Gr.:*** Aminotrophylle-88; Arterosol†; Cebragil; Latys; Lobelo; Meclivin†; Meditam†; Noforit; Nootrop; Oxynium; Piracem; Stamin; ***Hong Kong:*** Nootropil; Piratin; ***Hung.:*** Cerebryl; Lucetam; Memoril; Nootropil; Pirabene; Pyramen†; ***India:*** Nootropil; Normenta; Pirament; Piratam†; ***Indon.:*** Antikun; Benocetam; Cetoros; Chepamed; Ciclobrain; Encebion; Ethopil; Fepiram; Gotropil; Gracetam; Latropil; Lutrotam; Mersitropil; Neurocet; Neurotam; Noocephal; Nootropil; Nufacetam; Piratrof; Pratropil; Primatam; Procetam; Resibron; Revolan; Scantropil; Sotropil; Tropilex; ***Ital.:*** Cerebropan†; Nootropil; Norzetam†; Psycoton; ***Jpn:*** Myocalm; Nootropil; ***Malaysia:*** Cebrotonin†; Knowful; Nootropil; ***Mex.:*** Dinagen; Nootropil; ***Neth.:*** Nootropil; ***Norw.:*** Nootropil; ***Philipp.:*** Irahex; Nootropil; ***Pol.:*** Lucetam; Memotropil; Nootropil; ***Port.:*** Acetar; Noostan; Nootropil; Oxibran; Stimubral†; ***Rus.:*** Lucetam (Луцетам); Memotropil (Мемотропил); Nootropil (Ноотропил); Phezam (Фезам); Piratropil (Пиратропил); ***S.Afr.:*** Nootropil; ***Singapore:*** Cebrotonin; Cetam†; Nootropil; Piratam; Racetam; ***Spain:*** Ciclofalina; Nootropil; ***Swed.:*** Nootropil; ***Switz.:*** Nootropil; Pirax; ***Thai.:*** Embol; Mempil; Nocetam; Nootropil; Scarda; ***Turk.:*** Nootropil; Norotrop; ***UK:*** Nootropil; ***Venez.:*** Breinox; Nootropil†.

Multi-ingredient: ***Braz.:*** Energiclin; Energivit; Exit; Isketam; Vincetron†; ***Port.:*** Anacervix; Centracetam†; Euvifor†; Stimilfar†; ***Rus.:*** Omaron (Омарон); Piracezine (Пирацезин); Vinpotropile (Винпотропил); ***Spain:*** Anacervix; Devincal; Diemil; Piracetam Complex†; ***Venez.:*** Devincal†.