Orphenadrine Citrate *(BANM, rINNM)*

Citrato de orfenadrina; Mephenamine Citrate; Orfenadriinisitraatti; Orfenadrincitrat; Orfenadrin-citrát; Orfenadrino citratas; Orphenadin Citrate; Orphénadrine, Citrate d'; Orphénadrine, citrate de; Orphenadrini citras. (*RS*)-Dimethyl[2-(2-methylbenzhydryloxy)ethyl]amine dihydrogen citrate.

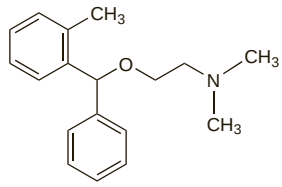
Орфенадрина Цитрат

$C_{18}H_{23}NO,C_6H_8O_7$ = 461.5.

CAS — 83-98-7 (orphenadrine); 4682-36-4 (orphenadrine citrate).

ATC — M03BC01.

ATC Vet — QM03BC01.



(orphenadrine)

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.

Ph. Eur. 6.2 (Orphenadrine Citrate). A white or almost white crystalline powder. Sparingly soluble in water; slightly soluble in alcohol. Protect from light.

USP 31 (Orphenadrine Citrate). A white, practically odourless, crystalline powder. Sparingly soluble in water; slightly soluble in alcohol; insoluble in chloroform, in ether, and in benzene. Store in airtight containers. Protect from light.

Orphenadrine Hydrochloride *(BANM, rINNM)*

BS-5930; Hidrocloruro de orfenadrina; Mephenamine Hydrochloride; Orfenadriinihydrokloridi; Orfenadrin-hidrokloridi; Orfenadrin-hydrochlorid; Orfenadrinhydroklorid; Orfenadrino hidrochloridas; Orphenadin Hydrochloride; Orphénadrine, Chlorhydrate d'; Orphénadrine, chlorhydrate de; Orphenadrini hydrochloridum. (*RS*)-Dimethyl[2-(2-methylbenzhydryloxy)ethyl]-amine hydrochloride.

Орфенадрина Гидрохлорид

$C_{18}H_{23}NO,HCl$ = 305.8.

CAS — 341-69-5.

ATC — N04AB02.

ATC Vet — QN04AB02.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Orphenadrine Hydrochloride). A white or almost white crystalline powder. Freely soluble in water and in alcohol. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219. Orphenadrine may cause insomnia.

Abuse. A 23-year-old schizophrenic man, whose treatment included orphenadrine 100 mg three times daily, obtained illicit supplies and increased the dose for euphoric effect.[1] On one occasion he had an epileptic convulsion after a 600-mg dose.

See also under Trihexyphenidyl Hydrochloride, p.820.

1. Shariatmadari ME. Orphenadrine dependence. *BMJ* 1975; **3:** 486.

Overdosage. A report[1] of acute poisoning with orphenadrine after massive overdosage in a schizophrenic patient, who responded to intensive supportive treatment, including large doses of adrenaline, dopamine, and dobutamine to restore blood pressure following asystole. Between 1977 and 1980 twelve deaths due to orphenadrine were recorded by the UK National Poisons Unit.

1. Clarke B, *et al*. Acute poisoning with orphenadrine. *Lancet* 1985; **i:** 1386.

Porphyria. Orphenadrine has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Withdrawal. A suspected withdrawal syndrome was reported in a 56-year-old woman who showed slow neurological postoperative recovery after her orphenadrine treatment had been stopped abruptly;[1] her status improved when the drug was restarted.

1. Esler MD, *et al*. Postoperative orphenadrine withdrawal. *Br J Anaesth* 2000; **85:** 497.

Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220). Orphenadrine is an inhibitor of the cytochrome P450 isoenzyme CYP2B6, which is involved in the metabolism of bupropion to its major metabolite; licensed product information advises that orphenadrine should be used with caution in patients also receiving bupropion.

Chlorpromazine. For the effect of orphenadrine on plasma concentrations of chlorpromazine, see Antiparkinsonian Drugs, p.974.

Dextropropoxyphene. A suggested interaction between orphenadrine and dextropropoxyphene was open to question.[1,2]

1. Pearson RE, Salter FJ. Drug interaction? — orphenadrine with propoxyphene. *N Engl J Med* 1970; **282:** 1215.
2. Puckett WH, Visconti JA. Orphenadrine and propoxyphene (cont.). *N Engl J Med* 1970; **283:** 544.

Pharmacokinetics

Orphenadrine is readily absorbed from the gastrointestinal tract and after intramuscular injection. It is almost completely metabolised to at least 8 metabolites. It is mainly excreted in the urine as metabolites and small amounts of unchanged drug. The half-life of orphenadrine has been reported to be 14 hours (but see below).

Half-life. While the mean elimination half-life of orphenadrine in 5 healthy subjects given a single dose of the hydrochloride was found to be 15.5 hours, elimination half-lives of 30.5 and 40 hours were calculated in 2 patients given repeated oral doses.[1]

1. Labout JJM, *et al*. Difference between single and multiple dose pharmacokinetics of orphenadrine hydrochloride in man. *Eur J Clin Pharmacol* 1982; **21:** 343–50.

Uses and Administration

Orphenadrine, which is a congener of diphenhydramine (p.577) without sharing its soporific effect, is a tertiary amine antimuscarinic with actions and uses similar to those of trihexyphenidyl (p.820). It also has weak antihistaminic and local anaesthetic properties. Orphenadrine is used as the hydrochloride and the citrate; doses are expressed in terms of the relevant salt.

Orphenadrine is used as the hydrochloride in the symptomatic treatment of **parkinsonism** (p.791), including the alleviation of the extrapyramidal syndrome induced by drugs such as phenothiazines, but, like other antimuscarinics, is of no value against tardive dyskinesias. The initial oral dose of orphenadrine hydrochloride is 150 mg daily in divided doses gradually increased by 50 mg every 2 or 3 days according to response; the usual maintenance dose is in the range of 150 to 300 mg daily, but some patients may require a total of up to 400 mg daily. Orphenadrine hydrochloride has also been given intramuscularly.

Orphenadrine is also used as the citrate to relieve pain due to **skeletal muscle spasm**. It is given orally in a dose of 100 mg twice daily or by intramuscular or slow intravenous injection in a dose of 60 mg which has been repeated every 12 hours.

Combinations of orphenadrine with an NSAID, usually diclofenac, or with paracetamol, have been used in the treatment of musculoskeletal and joint disorders.

Hiccup. Orphenadrine citrate has been used in some countries for the treatment of intractable hiccup. For the management of intractable hiccups see under Chlorpromazine, p.976.

Muscle and joint disorders. References to the use of orphenadrine in the management of leg cramps and other painful conditions associated with skeletal muscle spasm,[1,2] and with diclofenac in osteoarthritis and other musculoskeletal disorders.[3,4]

1. Latta D, Turner E. An alternative to quinine in nocturnal leg cramps. *Curr Ther Res* 1989; **45:** 833–7.
2. Hunskaar S, Donnell D. Clinical and pharmacological review of the efficacy of orphenadrine and its combination with paracetamol in painful conditions. *J Int Med Res* 1991; **19:** 71–87.
3. Uitz E, *et al*. Diclofenac/Orphenadrin-Infusionstherapie bei Patienten mit aktivierten Arthrosen. *Wien Med Wochenschr* 1998; **148:** 179–82.
4. Aglas F, *et al*. Ergebnisse einer Anwendungsbeobachtung mit Diclofenac/Orphenadrin-Infusionen bei Patienten mit muskuloskelettalen Krankheiten und Funktionsstorungen. *Acta Med Austriaca* 1998; **25:** 86–90.

Preparations

BP 2008: Orphenadrine Hydrochloride Tablets;
USP 31: Orphenadrine Citrate Injection.

Proprietary Preparations (details are given in Part 3)
Austral.: Norflex; ***Belg.:*** Disipal; ***Canad.:*** Norflex; ***Chile:*** Plenactol; ***Denm.:*** Disipal; Lysantin; Norflex†; ***Fin.:*** Norflex; ***Ger.:*** Norflex; ***Gr.:*** Disipal; Norflex; ***India:*** Orphipal; ***Israel:*** Flexin; ***Ital.:*** Disipal; ***Malaysia:*** Norflex; ***Mex.:*** Norflex; ***Norw.:*** Disipal†; ***NZ:*** Disipal; Norflex; ***Port.:*** Norflex†; ***S.Afr.:*** Disipal; Norflex; Phenerine; ***Swed.:*** Disipal†; Norflex; ***Thai.:*** Norflex; Orfenal†; ***UK:*** Biorphen; Disipal; ***USA:*** Banflex; Flexon; Norflex; ***Venez.:*** Norflex.

Multi-ingredient: ***Arg.:*** Belmalen; Doloctaprin Plus†; Flogodisten; Metaflex Plus†; Mio Aldoron; Mio-Virobron; ***Austral.:*** Norgesic; ***Austria:*** Neodolpasse; Norgesic; ***Braz.:*** Anapirol†; Banidor†; Dalgex; Doralgex; Dorciflex; Dorflex; Doricin; Dorzone; Flexalgex; Flexdor; Itaiflex†; Miorrelax; Nevralgex; Relaflex; Rielex; Sedalex; Theopirina†; ***Canad.:*** Norgesic; ***Chile:*** Norgesic; ***Cz.:*** Neodolpasse; ***Fin.:*** Dolan; Norgesic; ***Ger.:*** Norgesic N†; ***Gr.:*** Norgesic; ***Hong Kong:*** Norgesic; ***Hung.:*** Neodolpasse; ***Irl.:*** Norgesic†; ***Israel:*** Muscol; Norgesic; ***Malaysia:*** Anarex; Norgesic; Orphenadol; Suniton; ***Mex.:*** Norflex Plus; ***NZ:*** Norgesic; ***Philipp.:*** Norgesic; ***Port.:*** Norgesic†; ***S.Afr.:*** Besemax; Besenol; Norflex Co; ***Singapore:*** Anarex; Camgesic; Norgesic; Norphen; Orphenadol; ***Swed.:*** Norgesic; ***Thai.:*** Cenasic; Conlax†; Dorpane; Med-Myolax†; Medgesic; Muscol†; Myodrine; Myoflex; Myosic; Myospa; Nabesac; Neosec; Norgesic; Norgic; Norphen; Nuosic; Nurasic; Orano; Orflex; Orpar; Orphengesic; Parina; Poli-Relaxane; Polydol; Pormus; Relar; Rena; ***UAE:*** Muscadol; ***USA:*** Norgesic; Orphengesic; ***Venez.:*** Norgesic.

Pergolide Mesilate *(BANM, rINNM)*

LY-127809; Mesilato de pergolida; Pergolid Mesilat; Pergolid mesylát; Pergolide, mésilate de; Pergolide Mesylate *(USAN)*; Pergolidi mesilas; Pergolidimesilaatti; Pergolidmesilat; Pergolid-mezilát; Pergolido mesilatas. 8β-Methylthiomethyl-6-propylergoline methanesulphonate; Methyl (8*R*,10*R*)-6-propylergolin-8-ylmethyl sulphide methanesulphonate.

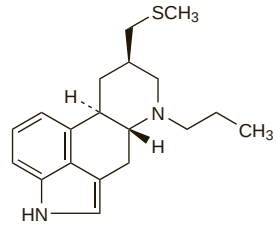
Перголида Мезилат

$C_{19}H_{26}N_2S,CH_4O_3S$ = 410.6.

CAS — 66104-22-1 (pergolide); 66104-23-2 (pergolide mesilate).

ATC — N04BC02.

ATC Vet — QN04BC02.



(pergolide)

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.

Ph. Eur. 6.2 (Pergolide Mesilate). A white or almost white crystalline powder. Slightly soluble in water, in alcohol, and in dichloromethane; very slightly soluble in acetone; sparingly soluble in methyl alcohol. Protect from light.

USP 31 (Pergolide Mesylate). A white to off-white powder. Slightly soluble in water, in dehydrated alcohol, and in chloroform; very slightly soluble in acetone; practically insoluble in ether; sparingly soluble in methyl alcohol. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Bromocriptine, p.798.

An increased incidence of uterine neoplasms has been reported in *rodents* given high doses of pergolide mesilate.

Effects on mental function. For reports of daytime somnolence occurring in patients receiving dopamine agonists including pergolide, see under Adverse Effects of Levodopa, p.805.

Fibrosis. For reports of fibrotic reactions occurring in patients with Parkinson's disease receiving ergot derivative dopamine agonists including pergolide, see under Adverse Effects of Bromocriptine, p.799.

In Australia,[1] Canada,[2], and Europe[3] regulatory authorities recommended that patients undergo a cardiovascular evaluation before starting treatment with pergolide; periodic clinical monitoring for development of valvular disease or fibrosis is also recommended. Doses of pergolide above 3 mg daily are not recommended by the EMEA.[3] Furthermore, use is restricted to patients who are intolerant of, or who fail to respond to, non-ergot drug treatment and it is contra-indicated in patients with a history of fibrotic disorders or in those with anatomical evidence of cardiac valvulopathy.[4] In 2007, based on further evidence from 2 studies,[5,6] pergolide was withdrawn from the market in the USA[7] and Canada.[8]

1. Adverse Drug Reactions Advisory Committee (ADRAC). Cardiac valvulopathy with pergolide. *Aust Adverse Drug React Bull* 2004; **23:** 14. Also available at: http://www.tga.gov.au/adr/aadrb/aadr0408.pdf (accessed 16/02/06)

2. Shire, Canada. New Safety information regarding Permax and occurrence of cardiac valvulopathy/fibrosis: update on the use of Permax (pergolide mesylate) (issued 12/10/04). Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/shire_permax_2_hpc-cps-eng.pdf (accessed 12/08/08)

3. EMEA. EMEA recommends new warnings and contraindications for ergot-derived dopamine agonists (issued 26th June, 2008). Available at: http://www.emea.europa.eu/pdfs/human/press/pr/32239508en.pdf (accessed 08/08/08)

4. MHRA. Dopamine agonists for Parkinson's disease (issued 30th March 2007). Available at: http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Product-specificinformationandadvice/DopamineagonistsforParkinson146sdisease/CON2030729 (accessed 03/06/08)

5. Schade R, *et al.* Dopamine agonists and the risk of cardiac-valve regurgitation. *N Engl J Med* 2007; **356:** 29–38.

6. Zanettini R, *et al.* Valvular heart disease and the use of dopamine agonists for Parkinson's disease. *N Engl J Med* 2007; **356:** 39–46.

7. FDA. FDA public health advisory: pergolide (marketed as Permax) (issued 29th March 2007). Available at: http://www.fda.gov/cder/drug/advisory/pergolide.htm (accessed 03/06/08)

8. Eli Lilly, Canada. Health Canada-mandated important safety information on Permax (pergolide mesylate) (issued 10th August 2007). Available at: http://www.lilly.ca/searchable/media/hcp/permax.pdf (accessed 25/06/08)

Interactions

As for Bromocriptine, p.800.

Pharmacokinetics

Pergolide mesilate is absorbed from the gastrointestinal tract. It is reported to be about 90% bound to plasma proteins. It is excreted mainly in the urine in the form of metabolites.

◊ References.

1. Blin O. The pharmacokinetics of pergolide in Parkinson's disease. *Curr Opin Neurol* 2003; **16** (suppl 1): S9–S12.

Uses and Administration

Pergolide mesilate, an ergot derivative, is a dopamine D_2-agonist with actions and uses similar to those of bromocriptine (p.800), but in contrast to bromocriptine (a dopamine D_2-agonist) it also has agonist properties at D_1 and D_3 receptors. Pergolide is used in the management of Parkinson's disease as monotherapy, or as an adjunct to levodopa therapy to reduce 'end-of-dose' or 'on-off' fluctuations in response; in the UK pergolide is restricted to patients who are intolerant of, or who fail to respond to, non-ergot drug treatment. Pergolide is given by mouth as the mesilate with doses expressed as the base. Pergolide mesilate 65.3 mg is equivalent to about 50 mg pergolide.

For use as *monotherapy* an initial dose equivalent to 50 micrograms of pergolide is given on the first evening of therapy. The dose is thereafter gradually increased: 50 micrograms twice daily is taken on days 2 to 4, then increased by 100 to 250 micrograms every 3 or 4 days, given in 3 divided doses, up to a daily dose of 1.5 mg at day 28. After day 30, the dose should be increased further by a maximum of 250 micrograms twice a week until an optimum response is achieved. Usual maintenance doses are 2.1 to 2.5 mg daily; doses above 3 mg daily are not recommended by the EMEA. The daily dose is usually given in 3 divided doses.

For use as *adjunctive therapy* with levodopa, pergolide should be introduced gradually and during this period patients can have their levodopa dosage decreased gradually until an optimum response is achieved. The initial dose of pergolide is the equivalent of 50 micrograms daily for the first 2 days, increased gradually by 100 or 150 micrograms every third day over the next 12 days of therapy. Further increases of 250 micrograms may then be made every third day until an optimum response is achieved. A usual maintenance dose is 3 mg daily; doses above 3 mg daily are not recommended by the EMEA. The daily dose is usually given in 3 divided doses.

Acromegaly. Dopaminergics can produce a paradoxical reduction in growth hormone secretion and may be used in the treatment of acromegaly as adjunctive therapy to surgery, radiotherapy, or somatostatin analogues to reduce circulating growth hormone levels, although they are less effective than somatostatin analogues (p.1798). While bromocriptine has been the main dopamine agonist used pergolide has also been tried.[1]

1. Kleinberg DL, *et al.* Pergolide for the treatment of pituitary tumors secreting prolactin or growth hormone. *N Engl J Med* 1983; **309:** 704–9.

Hyperprolactinaemia and prolactinomas. Dopamine agonists are widely used for the treatment of hyperprolactinaemia secondary to a prolactinoma (p.2079). Pergolide has been suggested as an alternative to bromocriptine in this condition.

Studies[1-3] of pergolide mesilate in patients with hyperprolactinaemia indicate that single doses reduce serum-prolactin concentrations for more than 24 hours. In most patients, the effective dose was between 50 and 150 micrograms daily. Adverse effects were similar to those seen with bromocriptine, although some patients who could not take bromocriptine were able to tolerate pergolide (and *vice versa*). Pergolide reportedly lost favour for this indication after reports of an increased incidence of uterine neoplasms in *rodents* receiving high doses. However, licensed product information states that no cases of uterine malignancies have to date been reported in humans receiving pergolide. The long-term outcome of treatment of macroprolactinomas with pergolide has been examined in 23 patients,[4] and efficacy and relative safety of pergolide was demonstrated after an average of 27 months (range: 9 to 64 months) treatment.

1. Franks S, *et al.* Treatment of hyperprolactinaemia with pergolide mesylate: acute effects and preliminary evaluation of long-term treatment. *Lancet* 1981; **ii:** 659–61.

2. Franks S, *et al.* Effectiveness of pergolide mesylate in long-term treatment of hyperprolactinaemia. *BMJ* 1983; **286:** 1177–9.

3. Kleinberg DL, *et al.* Pergolide for the treatment of pituitary tumors secreting prolactin or growth hormone. *N Engl J Med* 1983; **309:** 704–9.

4. Freda PU, *et al.* Long-term treatment of prolactin-secreting macroadenomas with pergolide. *J Clin Endocrinol Metab* 2000; **85:** 8–13.

Parkinsonism. Dopamine agonists such as pergolide are often used to begin the treatment of parkinsonism (p.791) in an attempt to delay therapy with levodopa, particularly in younger patients. They also have an adjunctive use when levodopa is no longer effective alone or cannot be tolerated, and may sometimes be useful in reducing 'off' periods with levodopa and in ameliorating other fluctuations in mobility in the later stages of the disease. Pergolide has a relatively long duration of action compared with other dopamine agonists commonly used. Although the duration of the clinical antiparkinsonian effect of pergolide remains to be determined, studies suggest it is of the order of 5 to 8 hours. Depending on the dose used the response to other dopamine agonists in late parkinsonism is 1 to 4 hours for levodopa, 2 to 4 hours for lisuride, and 4 to 6 hours for bromocriptine.

References.

1. Anonymous. Pergolide (Celance)—a third dopamine agonist. *Drug Ther Bull* 1991; **29:** 79.

2. Markham A, Benfield P. Pergolide: a review of its pharmacology and therapeutic use in Parkinson's disease. *CNS Drugs* 1997; **7:** 328–40.

3. Barone P, *et al.* Pergolide monotherapy in the treatment of early PD: a randomized, controlled study. *Neurology* 1999; **53:** 573–9.

4. Clarke CE, Speller JM. Pergolide for levodopa-induced complications in Parkinson's disease. Available in The Cochrane Database of Systematic Reviews, Issue 2. Chichester: John Wiley; 1999 (accessed 16/02/06).

5. Clarke CE, Speller JM. Pergolide versus bromocriptine for levodopa-induced complications in Parkinson's disease. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 1999 (accessed 16/02/06).

Restless legs syndrome. The aetiology of restless legs syndrome (see Sleep-associated Movement Disorders, p.958) is obscure and treatment has largely been empirical although dopaminergic therapy has emerged as a common first-line choice. Pergolide has produced some benefit in a number of studies.[1-6] In a randomised placebo-controlled study,[6] therapeutic effects were observed with mean daily doses of pergolide 400 micrograms after 6 weeks and maintained after 12 months with doses of up to 720 micrograms daily.

1. Silber MH, *et al.* Pergolide in the management of restless legs syndrome: an extended study. *Sleep* 1997; **20:** 878–82.

2. Winkelmann J, *et al.* Treatment of restless legs syndrome with pergolide—an open clinical trial. *Mov Disord* 1998; **13:** 566–9.

3. Earley CJ, *et al.* Randomized, double-blind, placebo-controlled trial of pergolide in restless legs syndrome. *Neurology* 1998; **51:** 1599–1602.

4. Wetter TC, *et al.*. A randomized controlled study of pergolide in patients with restless legs syndrome. *Neurology* 1999; **52:** 944–50.

5. Stiasny K, *et al.* Long-term effects of pergolide in the treatment of restless legs syndrome. *Neurology* 2001; **56:** 1399–1402.

6. Trenkwalder C, *et al.* Efficacy of pergolide in treatment of restless legs syndrome: the PEARLS study. *Neurology* 2004; **62:** 1391–7.

Tourette's syndrome. Pergolide has been studied in the management of Tourette's syndrome (see Tics, p.954). A preliminary study[1] produced encouraging results, subsequently confirmed by placebo-controlled trials in children and adolescents.[2,3]

1. Lipinski JF, *et al.* Dopamine agonist treatment of Tourette disorder in children: results of an open-label trial of pergolide. *Mov Disord* 1997; **12:** 402–7.

2. Gilbert DL, *et al.* Tourette's syndrome improvement with pergolide in a randomized, double-blind, crossover trial. *Neurology* 2000; **54:** 1310–15.

3. Gilbert DL, *et al.* Tic reduction with pergolide in a randomized controlled trial in children. *Neurology* 2003; **60:** 606–11.

Preparations

USP 31: Pergolide Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Aroltex; Breator†; Celance; Geranil†; Parlide†; ***Austral.:*** Permax; ***Austria:*** Permax; ***Belg.:*** Permax; ***Braz.:*** Celance; ***Canad.:*** Permax; ***Chile:*** Celance†; ***Cz.:*** Permax; ***Denm.:*** Permax; ***Fin.:*** Permax; ***Fr.:*** Celance; ***Ger.:*** Parkotil; ***Gr.:*** Celance; ***Hong Kong:*** Celance†; ***Hung.:*** Parkotil†; ***Irl.:*** Celance; ***Ital.:*** Nopar; ***Mex.:*** Permax; ***Neth.:*** Permax; ***NZ:*** Permax; ***Pol.:*** Hizest†; ***Port.:*** Permax; ***S.Afr.:*** Permax; ***Singapore:*** Celance†; ***Spain:*** Pharken; ***Switz.:*** Permax; ***Thai.:*** Celance†; ***Turk.:*** Permax; ***UK:*** Celance; ***USA:*** Permax†.

Piribedil *(rINN)*

ET-495; EU-4200; Piribédil; Piribedilum. 2-(4-Piperonylpiperazin-1-yl)pyrimidine.

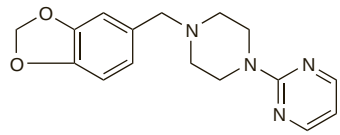
Пирибедил

$C_{16}H_{18}N_4O_2$ = 298.3.

CAS — 3605-01-4.

ATC — N04BC08.

ATC Vet — QN04BC08.



Profile

Piribedil is a non-ergot dopamine agonist that has been given orally in the treatment of parkinsonism and in circulatory disorders. Piribedil mesilate has been given by injection for circulatory disorders. Preparations of piribedil are licensed in some countries for the management of impaired memory and cognitive function in the elderly.

Adverse effects reported include nausea and vomiting, dizziness, hallucinations, confusion, drowsiness, hypothermia, dyskinesias, and occasional changes in liver function.

When used as monotherapy in Parkinson's disease a usual daily oral dose of piribedil is 150 to 250 mg in divided doses; a daily dose of 80 to 140 mg may be suitable when used as an adjunct to levodopa.

Effects on mental function. For reports of daytime somnolence occurring in patients receiving dopamine agonists including piribedil, see under Adverse Effects of Levodopa, p.805.

Parkinsonism. Piribedil is a dopamine D_2-agonist while its metabolite is reported to act on D_1 receptors. It has been mainly used as an adjunct to levodopa therapy in the treatment of Parkinson's disease (p.791).

References.

1. Montastruc JL, *et al.* Current status of dopamine agonists in Parkinson's disease management. *Drugs* 1993; **46:** 384–93.

2. Montastruc JL, *et al.* A randomized, double-blind study of a skin patch of a dopaminergic agonist, piribedil, in Parkinson's disease. *Mov Disord* 1999; **14:** 336–41.

3. Ziegler M, Rondot P. Activité du piribédil dans la maladie de Parkinson: étude multicentrique. *Presse Med* 1999; **28:** 1414–18.

4. Ziegler M, *et al.* Efficacy of piribedil as early combination to levodopa in patients with stable Parkinson's disease: a 6-month, randomized, placebo-controlled study. *Mov Disord* 2003; **18:** 418–25.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Trivastal; ***Braz.:*** Trivastal; ***Fr.:*** Trivastal; ***Ger.:*** Trivastal; ***Gr.:*** Trivastal; ***India:*** Trivastal; ***Ital.:*** Trivastan; ***Malaysia:*** Trivastal; ***Philipp.:*** Trivastal; ***Pol.:*** Pronoran; ***Port.:*** Trivastal; ***Rus.:*** Pronoran (Пронoран); ***Singapore:*** Trivastal; ***Thai.:*** Trivastal; ***Turk.:*** Trivastal; ***Venez.:*** Trivastal.