Lisuride Maleate *(BANM, rINNM)*

Lisurid Maleat; Lisuride, Maléate de; Lisuridi Hydrogenomaleas; Lisuridi Maleas; Lisuridivetymaleaatti; Lisuridvätemaleat; Lysuride Maleate; Maleato de lisurida; Methylergol Carbamide Maleate. 3-(9,10-Didehydro-6-methylergolin-8α-yl)-1,1-diethylurea hydrogen maleate; 8-Decarboxamido-8-(3,3-diethylureido)-D-lysergamide maleate.

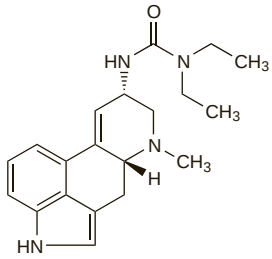
Лизурида Малеат

$C_{20}H_{26}N_4O,C_4H_4O_4$ = 454.5.

CAS — 18016-80-3 (lisuride); 19875-60-6 (lisuride maleate).

ATC — G02CB02; N02CA07.

ATC Vet — QG02CB02; QN02CA07.



(lisuride)

Adverse Effects and Precautions

As for Bromocriptine, p.798. Infusion of lisuride in parkinsonian patients has been associated with severe psychiatric adverse effects.

Effects on mental function. For reports of daytime somnolence occurring in patients receiving dopamine agonists including lisuride, 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 lisuride, see under Adverse Effects of Bromocriptine, p.799.

Porphyria. Lisuride maleate is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Interactions

As for Bromocriptine, p.800.

Pharmacokinetics

◊ Plasma concentrations varied widely after a single oral dose of lisuride maleate 300 micrograms in 11 patients with Parkinson's disease.[1] Absorption was rapid and the mean plasma elimination half-life was 2.2 hours. Only a mean of 0.05% of the dose was excreted unchanged in the urine in 24 hours. The mean oral bioavailability of lisuride maleate has been reported[2] to be 10% after a 100-microgram dose and 22% after a 300-microgram dose.

A single dose of lisuride 25 micrograms given by intravenous, intramuscular, or subcutaneous injection reduced plasma-prolactin concentrations by up to 60% in 11 of 12 healthy subjects, the effect lasting for about 10 hours.[3] Plasma-lisuride concentrations after intravenous injection fell in 2 phases with half-lives of 14 minutes and 1.5 hours, respectively. Peak plasma concentrations after subcutaneous and intramuscular injection were obtained after 12 and 15 minutes, respectively.

1. Burns RS, *et al*. Disposition of oral lisuride in Parkinson's disease. *Clin Pharmacol Ther* 1984; **35:** 548–56.
2. Hümpel M, *et al*. Radioimmunoassay of plasma lisuride in man following intravenous and oral administration of lisuride hydrogen maleate; effect on plasma prolactin level. *Eur J Clin Pharmacol* 1981; **20:** 47–51.
3. Krause W, *et al*. The pharmacokinetics and pharmacodynamics of lisuride in healthy volunteers after intravenous, intramuscular, and subcutaneous injection. *Eur J Clin Pharmacol* 1991; **40:** 399–403.

Uses and Administration

Lisuride maleate, an ergot derivative, is a dopamine D_2-agonist with actions and uses similar to those of bromocriptine (p.798). It is also reported to have serotonergic activity. It is used similarly in the management of Parkinson's disease and has been used in disorders associated with hyperprolactinaemia. It is also used to suppress puerperal lactation for medical reasons; it is not recommended for the routine suppression of physiological lactation or for the treatment of postpartum breast pain and engorgement that can be adequately relieved with simple analgesics and breast support. Lisuride has been used in some countries for the treatment of acromegaly, and for the prophylaxis of migraine.

In the management of **Parkinson's disease** lisuride maleate has been given alone or added to treatment in patients having 'on-off' fluctuations in control with levodopa. It is normally given orally; doses should be taken with food. Initially 200 micrograms is taken at bedtime and additional doses of 200 micrograms may be added, at intervals of one week, first at midday and then in the morning. Further increases are made, until an optimum response is obtained, by adding 200 micrograms each week using the same sequence of increases, starting with the bedtime dose; dosage should not normally exceed 5 mg daily in 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, lisuride has been used in some countries, typically in a dose of 100 micrograms three times daily.

Hyperprolactinaemia and prolactinomas. Dopamine agonists have been widely used for the treatment of hyperprolactinaemia secondary to a prolactinoma (p.2079). Lisuride has been used as an alternative to bromocriptine. There is a report of plasma-prolactin concentrations being reduced to normal in 4 female patients with macroprolactinomas given lisuride 400 to 800 micrograms daily for 2 years.[1] Subsequent dosage reduction in 3 was followed by a rise in prolactin values. In the fourth patient prolactin remained in the normal range when the dose was progressively reduced from 400 to 50 micrograms daily, although complete withdrawal was followed by an increase in prolactin concentration within 3 months.

Vaginal dosage of lisuride has been studied in an attempt to avoid adverse effects associated with oral therapy. In a study[2] involving 40 women with hyperprolactinaemia a 200-microgram standard oral tablet placed in the vagina at night produced a similar reduction in prolactin concentrations to that obtained with 400 micrograms taken orally and was better tolerated.

1. Liuzzi A, *et al*. Low doses of dopamine agonists in the long-term treatment of macroprolactinomas. *N Engl J Med* 1985; **313:** 656–9.
2. Tasdemir M, *et al*. Vaginal lisuride for hyperprolactinaemia. *Lancet* 1995; **346:** 1362.

Lactation inhibition. Lisuride is used in some countries for the prevention of puerperal lactation (p.2003). However, the routine use of dopaminergics is not recommended for the suppression of physiological lactation.

References.

1. Venturini PL, *et al*. Effects of lisuride and bromocriptine on inhibition of lactation and on serum prolactin levels: comparative double-blind study. *Eur J Obstet Gynecol Reprod Biol* 1981; **11:** 395–400.

Mastalgia. In a small placebo-controlled study,[1] lisuride 200 micrograms daily was effective in the treatment of cyclical mastalgia. However, since mastalgia (p.2092) can improve spontaneously, treatment should rarely be considered unless pain has been present for about 6 months.

1. Kaleli S, *et al*. Symptomatic treatment of premenstrual mastalgia in premenopausal women with lisuride maleate: a double-blind placebo-controlled randomized study. *Fertil Steril* 2001; **75:** 718–23.

Migraine. Although lisuride has been used in some countries for the prophylaxis of migraine (p.616) it is not usually considered to be the drug of choice or even one of the main alternatives.

Parkinsonism. While some neurologists use dopamine agonists such as lisuride early in the treatment of parkinsonism (p.791) in an attempt to delay therapy with levodopa, others reserve them for adjunctive use when levodopa is no longer effective alone or cannot be tolerated. They are sometimes useful in reducing 'off' periods with levodopa and in ameliorating other fluctuations in mobility in the later stages of the disease.

References.

1. Rinne UK. Lisuride, a dopamine agonist in the treatment of early Parkinson's disease. *Neurology* 1989; **39:** 336–9.
2. Clarke CE, Speller JM. Lisuride for levodopa-induced complications in Parkinson's disease. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 1999 (accessed 16/02/06).
3. Clarke CE, Speller JM. Lisuride versus bromocriptine for levodopa-induced complications in Parkinson's disease. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 1999 (accessed 16/02/06).
4. Allain H, *et al.* Five-year follow-up of early lisuride and levodopa combination therapy versus levodopa monotherapy in de novo Parkinson's disease. *Eur Neurol* 2000; **44:** 22–30.

ADMINISTRATION. Lisuride has been of benefit when given by continuous intravenous or subcutaneous infusion in patients having fluctuations in mobility with levodopa therapy[1-4] but severe psychiatric effects have been associated with the use of these routes.[3] Transdermal lisuride is also being investigated for the treatment of Parkinson's disease and restless legs syndrome.[5,6]

1. Obeso JA, *et al.* Intravenous lisuride corrects oscillations of motor performance in Parkinson's disease. *Ann Neurol* 1986; **19:** 31–5.
2. Obeso JA, *et al*. Lisuride infusion pump: a device for the treatment of motor fluctuations in Parkinson's disease. *Lancet* 1986; **i:** 467–70.
3. Critchley P, *et al.* Psychosis and the lisuride pump. *Lancet* 1986; **i:** 349.
4. Stocchi F, *et al.* Prospective randomized trial of lisuride infusion versus oral levodopa in patients with Parkinson's disease. *Brain* 2002; **125:** 2058–66.
5. Woitalla D, *et al.* Transdermal lisuride delivery in the treatment of Parkinson's disease. *J Neural Transm Suppl* 2004; **68:** 89–95.
6. Benes H. Transdermal lisuride: short-term efficacy and tolerability study in patients with severe restless legs syndrome. *Sleep Med* 2006; **7:** 31–5.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Dopagon†; ***Austria:*** Dopergin; Prolacam†; ***Fr.:*** Arolac; Dopergine; ***Ger.:*** Cuvalit†; Dopergin; ***Gr.:*** Dipergon; ***Ital.:*** Dopergin; ***Mex.:*** Dopergin; ***Neth.:*** Dopergin; ***NZ:*** Dopergin; ***Spain:*** Dopergin; ***Switz.:*** Dopergin†; ***Thai.:*** Dopergin†; ***Turk.:*** Dopergin.

Metixene Hydrochloride *(BANM, rINNM)*

Hidrocloruro de metixeno; Methixene Hydrochloride *(USAN)*; Methixene Hydrochloride Monohydrate; Metikseenihydrokloridi; Metikseno hidrochloridas; Métixène, chlorhydrate de; Metixén-hidroklorid; Metixen-hydrochlorid monohydrát; Metixenhydroklorid; Metixeni hydrochloridum; Metixeni Hydrochloridum Monohydricum; NSC-78194; SJ-1977. (*RS*)-9-(1-Methyl-3-piperidylmethyl)thioxanthene hydrochloride monohydrate.

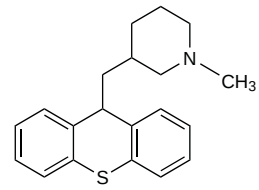
Метиксена Гидрохлорид

$C_{20}H_{23}NS,HCl,H_2O$ = 363.9.

CAS — 4969-02-2 (metixene); 1553-34-0 (anhydrous metixene hydrochloride); 7081-40-5 (metixene hydrochloride monohydrate).

ATC — N04AA03.

ATC Vet — QN04AA03.



(metixene)

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

Ph. Eur. 6.2 (Metixene Hydrochloride). A white or almost white, crystalline or fine crystalline powder. Soluble in water, in alcohol, and in dichloromethane. A 1.8% solution in water has a pH of 4.4 to 5.8. Protect from light.

Profile

Metixene hydrochloride is a tertiary antimuscarinic with actions similar to those of atropine (p.1219); it also has antihistaminic and direct antispasmodic properties.

It is used for 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 usual oral dose of metixene hydrochloride is 2.5 mg three times daily initially, gradually increased according to response to a total of 15 to 60 mg daily in divided doses.

Metixene hydrochloride has also been used in preparations to relieve gastrointestinal spasms.

Preparations

Proprietary Preparations (details are given in Part 3)

Ger.: Tremarit; ***Hung.:*** Tremaril; ***Ital.:*** Tremaril; ***Swed.:*** Tremoquil†.

Multi-ingredient: ***Philipp.:*** Spasmo-Canulase; ***Port.:*** Espasmo Canulase; ***S.Afr.:*** Spasmo-Canulase; ***Switz.:*** Spasmo-Canulase.

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.

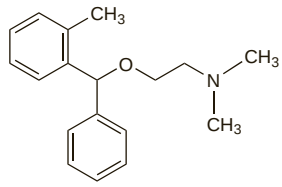
Орфенадрина Цитрат

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

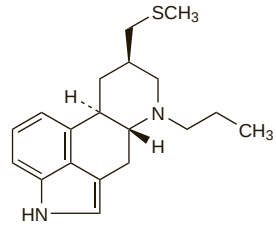
Перголида Мезилат

$C_{19}H_{26}N_2S,CH_4O_3S$ = 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)