Apomorphine Hydrochloride *(BANM)*

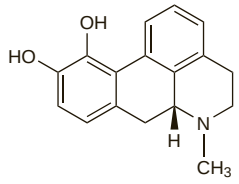
Apomorfiinihydrokloridi; Apomorfin Hidroklorür; Apomorfina, hidrocloruro de; Apomorfin-hidroklorid; Apomorfin-hydrochlorid hemihydrát; Apomorfinhydroklorid; Apomorfino hidrochloridas; Apomorfiny chlorowodorek; Apomorphine, chlorhydrate d'; Apomorphini hydrochloridum; Apomorphini Hydrochloridum Hemihydricum. 6aβ-Aporphine-10,11-diol hydrochloride hemihydrate; (*R*)-10,11-Dihydroxy-6a-aporphine hydrochloride hemihydrate; (6a*R*)-5,6,6a,7-Tetrahydro-6-methyl-4*H*-dibenzo[*de,g*]quinoline-10,11-diol hydrochloride hemihydrate.

$C_{17}H_{17}NO_2$,HCl,$\frac{1}{2}H_2O$ = 312.8.

CAS — 58-00-4 (apomorphine); 314-19-2 (anhydrous apomorphine hydrochloride); 41372-20-7 (apomorphine hydrochloride, hemihydrate).

ATC — G04BE07; N04BC07.

ATC Vet — QG04BE07; QN04BC07.



(apomorphine)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Ph. Eur. 6.2 (Apomorphine Hydrochloride). White or faintly yellow to green-tinged greyish crystals or crystalline powder, the green tinge becoming more pronounced on exposure to air and light. Sparingly soluble in water and in alcohol. A 1% solution in water has a pH of 4.0 to 5.0. Store in airtight containers. Protect from light.
USP 31 (Apomorphine Hydrochloride). Odourless, minute white or greyish-white, glistening crystals or white powder. It gradually acquires a green colour on exposure to light and air. Soluble 1 in 50 of water and 1 in 20 of water at 80°; soluble 1 in 50 of alcohol; very slightly soluble in ether and in chloroform. Its solutions are neutral to litmus. Store in airtight containers. Protect from light.

Stability. Aqueous solutions of apomorphine hydrochloride decompose on storage and should not be used if they turn green or brown or contain a precipitate.

Adverse Effects

Treatment of parkinsonism. Apomorphine usually produces nausea and vomiting when given in therapeutic doses but these effects can be controlled by treatment with domperidone or trimethobenzamide. Transient sedation can be common during the first few weeks of treatment. Increased salivation and perspiration have also been reported. Apomorphine can produce neuropsychiatric disturbances including increasing cognitive impairment, personality changes, confusion, and hallucinations. Signs of CNS stimulation including euphoria, lightheadedness, restlessness, tremor, tachycardia, and tachypnoea occur less frequently. Apomorphine may induce dyskinesias during 'on' periods in patients with parkinsonism and these may be severe enough to require stopping therapy; postural instability and falls may also be a problem. Transient orthostatic hypotension may also occur infrequently. Eosinophilia has occurred rarely. The use of apomorphine with levodopa may cause haemolytic anaemia and treatment may need to be stopped if this cannot be satisfactorily controlled through dosage adjustment. Induration, nodule formation, and panniculitis, sometimes leading to ulceration, often develops at the site of subcutaneous injection.

Management of erectile dysfunction. The most common adverse effects have been nausea, headache, and dizziness. Other effects reported include yawning, rhinitis, pharyngitis, somnolence, infection, pain, increased cough, flushing, taste disturbances, and sweating. Fainting and syncope (vasovagal syndrome) have also occurred.

Overdosage with apomorphine can produce persistent vomiting, respiratory depression, bradycardia, hypotension, and coma; death may occur.

Akinesia. A 60-year-old man who was being investigated for parkinsonian symptoms became totally immobile and mute 15 minutes after receiving apomorphine 4 mg subcutaneously.[1] He remained conscious but was drowsy and sweating. Similar profound akinesia occurred on rechallenge with 2- and 6-mg doses. A diagnosis of probable nigrostriatal degeneration was made as the patient had previously shown no improvement with levodopa, but the mechanism of the idiosyncratic reaction to apomorphine was unclear.

1. Jenkins JR, Pearce JMS. Paradoxical akinetic response to apomorphine in parkinsonism. *J Neurol Neurosurg Psychiatry* 1992; **55:** 414–15.

Effects on the heart. A 67-year-old man developed palpitations with cold perspiration and chest pain, in addition to asthenia, salivation, nausea and vomiting, 5 minutes after receiving 3 mg apomorphine subcutaneously. An ECG showed atrial fibrillation with a ventricular frequency of 140 beats/minute.[1]

1. Stocchi F, *et al.* Transient atrial fibrillation after subcutaneous apomorphine bolus. *Mov Disord* 1996; **11:** 584–5.

Effects on mental function. Severe confusion, hallucinations, and acute psychosis were reported in 4 of 6 parkinsonian patients given subcutaneous apomorphine.[1] Three of the 4 had previously experienced mental disturbances while receiving lisuride. However, other studies failed to note effects on mental function in parkinsonian patients given apomorphine[2,3] and it has been suggested that the risk of psychosis in patients with no history of confusion or hallucinations is low.[3] UK licensed product information notes that apomorphine has been reported to exacerbate neuropsychiatric disturbances in patients with parkinsonism.

1. Ruggieri S, *et al.* Side-effects of subcutaneous apomorphine in Parkinson's disease. *Lancet* 1989; **i:** 566.
2. Stibe CMH, *et al.* Subcutaneous apomorphine in parkinsonian on-off oscillations. *Lancet* 1988; **i:** 403–6.
3. Poewe W, *et al.* Side-effects of subcutaneous apomorphine in Parkinson's disease. *Lancet* 1989; **i:** 1084–5.

Hypersensitivity. Allergic reactions including contact dermatitis, severe rhinitis, and respiratory distress have been reported in 2 workers who came into contact with apomorphine powder.[1] Contact allergy has also been reported in a patient who developed a swollen nose and lips after intranasal use of apomorphine.[2] Skin testing in all these cases[1,2] gave a positive reaction to apomorphine. Biopsy of subcutaneous nodules, which develop at the site of injection in most patients using apomorphine subcutaneously, has not been able to clarify what type of reaction was responsible for the development of panniculitis.[3] Although the nodules may slowly resolve the sites are often unsuitable for reuse as absorption from them is unpredictable; concern has been expressed that this may limit long-term use of apomorphine.[3]

1. Dahlquist I. Allergic reactions to apomorphine. *Contact Dermatitis* 1977; **3:** 349–50.
2. van Laar T, *et al.* Nasolabiale allergische reactie op intranasale toediening van apomorfine bij de ziekte van Parkinson. *Ned Tijdschr Geneeskd* 1992; **136** (suppl 47): 26–7.
3. Acland KM, *et al.* Panniculitis in association with apomorphine infusion. *Br J Dermatol* 1998; **138:** 480–2.

Oedema. Severe reversible oedema of the lower limbs developed in a patient receiving subcutaneous apomorphine.[1] Oedema recurred when apomorphine was reintroduced, but to a lesser extent.

1. Vermersch P. Severe oedema after subcutaneous apomorphine in Parkinson's disease. *Lancet* 1989; **ii:** 802.

Stomatitis. Stomatitis, severe enough to warrant stopping treatment, occurred in 4 of 8 patients after 2 to 6 months of therapy with sublingual apomorphine.[1]

1. Montastruc JL, *et al.* Sublingual apomorphine in Parkinson's disease: a clinical and pharmacokinetic study. *Clin Neuropharmacol* 1991; **14:** 432–7.

Treatment of Adverse Effects

In the UK, domperidone is usually given to control nausea and vomiting when apomorphine is used in the management of Parkinson's disease; pretreatment with domperidone for at least 2 days is advised before starting treatment with apomorphine. Usually domperidone can be withdrawn gradually over several weeks or longer although some patients may need to continue treatment indefinitely. In the USA, trimethobenzamide hydrochloride is used similarly, beginning 3 days before starting apomorphine treatment.

In overdosage an opioid antagonist such as naloxone has been given to treat excessive vomiting, and CNS and respiratory depression.

◊ References.

1. Bonuccelli U, *et al.* Naloxone partly counteracts apomorphine side effects. *Clin Neuropharmacol* 1991; **14:** 442–9.

Precautions

Apomorphine should not be given to patients with respiratory or CNS depression, hypersensitivity to opioids, neuropsychiatric problems, or dementia. It should be used with caution in patients prone to nausea and vomiting or when vomiting is likely to pose a risk. Apomorphine should also be used with care in patients with pulmonary, cardiovascular, or endocrine disease or with renal or hepatic impairment. Extra care is needed when starting treatment in elderly or debilitated patients and in those with a history of orthostatic hypotension. Patients who experience dizziness, lightheadedness, or syncope should not drive or operate machinery.

Treatment of parkinsonism. Apomorphine is not suitable for use in patients who have an 'on' response to levodopa marred by severe dyskinesia, hypotonia, or psychiatric effects; it should also not be used in those with hepatic impairment. Periodic monitoring of hepatic, renal, haematopoietic, and cardiovascular function has been advised and the *BNF* recommends that patients receiving apomorphine with levodopa should be screened for haemolytic anaemia on starting treatment and then every 6 months. Patients who develop anaemia, or those who have continuing confusion or hallucinations during treatment with apomorphine require observation and dosage adjustment under specialist supervision; treatment may need to be stopped. Excessive daytime sleepiness and sudden onset of sleep may also occur with apomorphine and caution is advised when driving or operating machinery; patients who suffer such effects should not drive or operate machinery until the effects have stopped recurring.

Local subcutaneous reactions can sometimes be reduced by using sodium chloride 0.9% to dilute injection solutions, by rotating injection sites, and possibly by use of ultrasound in areas of nodularity and induration.

Management of erectile dysfunction. UK licensed product information has warned that drugs for erectile dysfunction should be used with caution in patients with anatomical penile deformity.

Interactions

Apomorphine should be used with caution in patients receiving antihypertensives or organic nitrates as it may potentiate their hypotensive effects. Enhanced hypotensive effects may also occur when alcohol is given with apomorphine. The therapeutic effects of apomorphine may be antagonised by antipsychotics and other drugs that act as CNS dopamine inhibitors. The effect of apomorphine is possibly enhanced by entacapone and memantine.

Antiemetics. *Domperidone* (in the UK) and *trimethobenzamide* (in the USA) are used with apomorphine to control nausea and vomiting when it is prescribed for the management of parkinsonism. However, whether other antiemetics may safely be used is less clear. US licensed product information contra-indicates the use of *ondansetron* and related 5-HT_3 antagonists with apomorphine, on the grounds that profound hypotension and loss of consciousness has been reported in patients given this combination. However, UK licensed product information makes no mention of such a contra-indication, and licensed information for lower-dose products used in the management of erectile dysfunction notes that on the basis of interaction studies, ondansetron hydrochloride or *prochlorperazine maleate* may safely be given to patients receiving apomorphine for this indication.

Pharmacokinetics

Apomorphine is well absorbed after subcutaneous injection but undergoes extensive first-pass hepatic metabolism when given by mouth and oral bioavailability is low. However, it is readily absorbed after sublingual doses and peak plasma concentrations are achieved in about 40 to 60 minutes; bioavailability is reported to be about 17 to 18% compared with subcutaneous injection. Apomorphine is about 90% bound to plasma proteins, mainly to albumin.

Apomorphine is extensively metabolised in the liver, primarily by conjugation with glucuronic acid or sulfate; the major metabolite is apomorphine sulfate. It is also demethylated to produce norapomorphine. Most of a dose is excreted in urine, mainly as metabolites.

◊ References.

1. Neef C, van Laar T. Pharmacokinetic-pharmacodynamic relationships of apomorphine in patients with Parkinson's disease. *Clin Pharmacokinet* 1999; **37:** 257–71.
2. Argiolas A, Hedlund H. The pharmacology and clinical pharmacokinetics of apomorphine SL. *BJU Int* 2001; **88** (suppl 3): 18–21.
3. LeWitt PA. Subcutaneously administered apomorphine: pharmacokinetics and metabolism. *Neurology* 2004; **62** (suppl 4): S8–S11.

Uses and Administration

Apomorphine is a morphine derivative with structural similarities to dopamine. It is a potent dopamine D_1- and D_2-receptor agonist used in the management of parkinsonism, especially in the control of the 'on-off' effect. It has also been used in the management of erectile dysfunction. Apomorphine is given as the hydrochloride and doses are expressed in terms of this salt. The regimen for parkinsonism given below applies to the UK preparation and doses are give subcutaneously; a similar preparation is available in the USA although the licensed maximum single and daily doses are less than those in the UK.

The optimal dose of apomorphine in the management of 'off' periods in **parkinsonism** should be established individually under specialist care. At least 2 days of pretreatment with the antiemetic domperidone is advised before starting apomorphine. After withholding antiparkinsonian therapy overnight to provoke an 'off' period, a test dose of 1 mg is given initially, followed by a second dose of 2 mg after 30 minutes, if necessary. Subsequent incremental increases should then be given at intervals of at least 40 minutes, as necessary, to determine the lowest dose producing a satisfactory motor response. Once the patient's normal antiparkinsonian therapy is re-established, the effective dose of apomorphine hydrochloride is given at the first signs of an 'off' period.

The dose and frequency are further adjusted according to response; patients typically require 3 to 30 mg daily in divided doses but individual injections should not be greater than 10 mg. Patients who require more than 10 injections daily or those whose overall control of symptoms remains unsatisfactory with intermittent injections may benefit from continuous subcutaneous infusion. The infusion is started at a rate of 1 mg/hour and this may be increased in steps of up to 0.5 mg/hour at intervals of not less than 4 hours to a maximum rate of 4 mg/hour. It is advised that infusions should only be given during waking hours and that the infusion site should be changed every 12 hours; 24-hour infusions are not advised unless there are severe night-time symptoms. Patients usually need to supplement the infusion with intermittent bolus injections but the recommended maximum total daily dose given by infusion and/or injection is 100 mg.

In the management of **erectile dysfunction** the usual initial dose has been 2 mg taken sublingually about 20 minutes before sexual activity. A dose of 3 mg was used on subsequent occasions if necessary with a minimum of 8 hours between doses. Reduced dosage is needed in patients with renal impairment (see below).

Apomorphine stimulates the chemoreceptor trigger zone in the brain and can produce emesis within a few minutes of a dose. However, the use of apomorphine for the induction of emesis in poisoning is considered dangerous owing to the risk of inducing protracted vomiting and shock, and is not recommended.

Administration in renal impairment. In the management of erectile dysfunction, the maximum dose of apomorphine hydrochloride has been limited to 2 mg sublingually in patients with severe renal impairment.

Erectile dysfunction. Apomorphine is among a wide range of drugs that has been used in the management of erectile dysfunction[1-5] (p.2179) with some beneficial results. It is usually given sublingually although it has also been given subcutaneously.[3] Inhaled apomorphine is also under investigation.

1. Heaton JPW, *et al.* Recovery of erectile function by the oral administration of apomorphine. *Urology* 1995; **45:** 200–6.
2. Dula E, *et al.* Efficacy and safety of fixed-dose and dose-optimization regimens of sublingual apomorphine versus placebo in men with erectile dysfunction. *Urology* 2000; **56:** 130–5.
3. Segraves RT, *et al.* Effect of apomorphine on penile tumescence in men with psychogenic impotence. *J Urol (Baltimore)* 1991; **145:** 1174–5.
4. Martinez R, *et al.* Clinical experience with apomorphine hydrochloride: the first 107 patients. *J Urol (Baltimore)* 2003; **170:** 2352–5.
5. Gontero P, *et al.* Clinical efficacy of apomorphine SL in erectile dysfunction of diabetic men. *Int J Impot Res* 2005; **17:** 80–5.

DIAGNOSIS. Test doses of subcutaneous apomorphine have been used in the differential diagnosis of parkinsonian syndromes,[1-4] to distinguish forms responsive to dopaminergics from other parkinsonian syndromes such as Wilson's disease, corticobasal degeneration, and diffuse Lewy-body dementia. Oral challenge with levodopa is still the best test of dopaminergic responsiveness[5,6] but apomorphine has proved of value in re-assessing patients who have become less responsive to levodopa.[1,4]

1. Barker R, *et al.* Subcutaneous apomorphine as a diagnostic test for dopaminergic responsiveness in parkinsonian syndromes. *Lancet* 1989; **i:** 675.
2. Oertel WH, *et al.* Apomorphine test for dopaminergic responsiveness. *Lancet* 1989; **i:** 1262–3.
3. Frankel JP, *et al.* Use of apomorphine to test for dopamine responsiveness in Wilson's disease. *Lancet* 1989; **ii:** 801–2.
4. Hughes AJ, *et al.* Apomorphine test to predict dopaminergic responsiveness in parkinsonian syndromes. *Lancet* 1990; **336:** 32–4.
5. Steiger MJ, Quinn NP. Levodopa challenge test in Parkinson's disease. *Lancet* 1992; **339:** 751–2.
6. Müller T, *et al.* Repeated rating improves value of diagnostic dopaminergic challenge tests in Parkinson's disease. *J Neural Transm* 2003; **110:** 603–9.

Parkinsonism. ***TREATMENT.*** Although apomorphine has produced benefit in Parkinson's disease (p.791) when given orally, the high doses required to overcome extensive first-pass hepatic metabolism (up to 1.4 g daily in one study[1]), were associated with uraemia. The use of apomorphine in Parkinson's disease has therefore been limited by the need for parenteral dosage. The current main use of apomorphine in Parkinson's disease is for the stabilisation of patients with 'on-off' fluctuations unresponsive to other dopamine agonists. It is usually given subcutaneously either by injection or infusion but a review[2] of the use of apomorphine in Parkinson's disease also discussed studies of rectal, sublingual, and intranasal use. Inhaled apomorphine is also under investigation.

1. Cotzias GC, *et al.* Treatment of Parkinson's disease with aporphines. *N Engl J Med* 1976; **294:** 567–72.
2. Koller W, Stacy M. Other formulations and future considerations for apomorphine for subcutaneous injection therapy. *Neurology* 2004; **62** (suppl 4): S22–S26.

Preparations

USP 31: Apomorphine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Apokinon†; Uprima†; ***Austral.:*** Apomine; ***Austria:*** APO-go; Ixense†; Uprima†; ***Belg.:*** Uprima†; ***Braz.:*** Uprima; ***Chile:*** Noc; Uprima†; ***Cz.:*** APO-go; Uprima†; ***Denm.:*** Uprima†; ***Fin.:*** Uprima†; ***Fr.:*** Apokinon†; Ixense†; Uprima†; ***Ger.:*** APO-go; Ixense†; Uprima†; ***Gr.:*** APO-go; Taluvian†; Uprima†; ***Hong Kong:*** Uprima†; ***Hung.:*** APO-go†; Uprima†; ***Irl.:*** Uprima†; ***Israel:*** APO-go; ***Ital.:*** Apofin; Ixense†; Taluvian†; Uprima†; ***Jpn:*** Ixense; ***Mex.:*** Taluvian; ***Neth.:*** APO-go; Uprima†; ***Norw.:*** Uprima†; ***NZ:*** Apomine; Uprima†; ***Port.:*** APO-go; Uprima†; ***S.Afr.:*** Uprima†; ***Spain:*** APO-go; Taluvian†; Uprima†; ***Swed.:*** Uprima†; ***Switz.:*** Uprima†; ***Thai.:*** Ixense†; ***Turk.:*** APO-go; ***UK:*** APO-go; Uprima†; ***USA:*** Apokyn; ***Venez.:*** Uprima†.

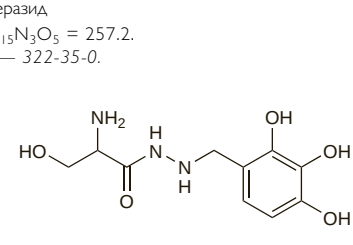
Benserazide *(BAN, USAN, rINN)*

Benseratsidi; Benserazid; Benserazida; Bensérazide; Benserazidum; Ro-4-4602. DL-Serine 2-(2,3,4-trihydroxybenzyl)hydrazide; 2-Amino-3-hydroxy-2'-(2,3,4-trihydroxybenzyl)propionohydrazide.

Бенсеразид

$C_{10}H_{15}N_3O_5$ = 257.2.

CAS — 322-35-0.



Benserazide Hydrochloride *(BANM, rINNM)*

Benseratsidihydrokloridi; Bensérazide, chlorhydrate de; Benserazid-hydrochlorid; Benserazidhydroklorid; Benserazidi hydrochloridum; Benserazido hidrochloridas; Benszerazid-hidroklorid; Hidrocloruro de benserazida; Serazide Hydrochloride.

Бенсеразида Гидрохлорид

$C_{10}H_{15}N_3O_5$,HCl = 293.7.

CAS — 14919-77-8; 14046-64-1.

NOTE. Compounded preparations of benserazide hydrochloride may be represented by the following names:

- Co-beneldopa *(BAN)*—benserazide 1 part and levodopa 4 parts (w/w).

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.*

Ph. Eur. 6.2 (Benserazide Hydrochloride). A white or yellowish-white or orange-white crystalline powder. It shows polymorphism. Freely soluble in water; very slightly soluble in dehydrated alcohol; practically insoluble in acetone. A 1% solution in water has a pH of 4.0 to 5.0. Protect from light.

Solubility. Benserazide is unstable in a neutral, alkaline, or strongly acidic medium.[1]

1. Schwartz DE, Brandt R. Pharmacokinetic and metabolic studies of the decarboxylase inhibitor benserazide in animals and man. *Arzneimittelforschung* 1978; **28:** 302–7.

Adverse Effects and Precautions

◊ Early reports[1] noted developmental abnormalities of the *rat* skeleton, but others found no evidence of any disorder involving bone metabolism in man.[2] Nevertheless licensed product information recommends that benserazide should not be given to patients under 25 years of age, nor to pregnant women or to women of child-bearing potential in the absence of adequate contraception.

1. Theiss E, Schärer K. Toxicity of L-dopa and a decarboxylase inhibitor in animal experiments. In: de Ajuriaguerra J, Gauthier G, eds. *Monoamines Noyaux Gris Centraux et Syndrome de Parkinson*. Geneva: Georg, 1971: 497–504.
2. Ziegler WH, *et al.* Toxicity of L-dopa and a dopa decarboxylase inhibitor in humans. In: de Ajuriaguerra J, Gauthier G, eds. *Monoamines Noyaux Gris Centraux et Syndrome de Parkinson*. Geneva: Georg, 1971: 505–16.

Pharmacokinetics

◊ Pharmacokinetic and metabolic studies[1,2] in *animals* and man have shown that, after oral doses in parkinsonian patients, benserazide was rapidly absorbed to the extent of about 58%; giving it with levodopa tended to increase this slightly. Benserazide was rapidly excreted in the urine in the form of metabolites, mostly within the first 6 hours; 85% of urinary excretion had occurred within 12 hours. It is mainly metabolised in the gut and appears to protect levodopa against decarboxylation primarily in the gut, but also in the rest of the organism, mainly by way of its metabolite trihydroxybenzylhydrazine. Benserazide did not cross the blood-brain barrier in *rats*.

1. Schwartz DE, *et al.* Pharmacokinetics of the decarboxylase benserazide in man: its tissue distribution in the rat. *Eur J Clin Pharmacol* 1974; **7:** 39–45.
2. Schwartz DE, Brandt R. Pharmacokinetic and metabolic studies of the decarboxylase inhibitor benserazide in animals and man. *Arzneimittelforschung* 1978; **28:** 302–7.

Uses and Administration

Benserazide hydrochloride is a peripheral dopa-decarboxylase inhibitor with actions similar to those of carbidopa (p.803) and is used similarly as an adjunct to levodopa in the treatment of parkinsonism (p.791). For details of dosage, see Levodopa, p.808.

◊ References.

1. Dingemanse J, *et al.* Pharmacodynamics of benserazide assessed by its effects on endogenous and exogenous levodopa pharmacokinetics. *Br J Clin Pharmacol* 1997; **44:** 41–8.

Preparations

BP 2008: Co-beneldopa Capsules; Dispersible Co-beneldopa Tablets.

Proprietary Preparations (details are given in Part 3)

Ger.: Restex.

Multi-ingredient: ***Arg.:*** Madopar; ***Austral.:*** Madopar; ***Austria:*** Dopamed; Levobens; Madopar; Restex; ***Belg.:*** Prolopa; ***Braz.:*** Prolopa; ***Canad.:*** Prolopa; ***Chile:*** Melitase; Prolopa; ***Cz.:*** Madopar; ***Denm.:*** Madopar; ***Fin.:*** Madopar; ***Fr.:*** Modopar; ***Ger.:*** Levodopa comp B; Levopar; Madopar; PK-Levo; ***Gr.:*** Madopar; ***Hong Kong:*** Madopar; ***Hung.:*** Madopar; ***Indon.:*** Leparson; Levazide; Levopar; Madopar; Pardoz; ***Irl.:*** Madopar; ***Israel:*** Levopar Plus; ***Ital.:*** Madopar; ***Malaysia:*** Madopar; ***Mex.:*** Madopar; ***Neth.:*** Madopar; Modopar; ***Norw.:*** Madopar; ***NZ:*** Madopar; ***Philipp.:*** Madopar; ***Pol.:*** Madopar; ***Port.:*** Madopar; ***Rus.:*** Madopar (Мадопар); ***S.Afr.:*** Madopar; ***Singapore:*** Madopar; ***Spain:*** Madopar; ***Swed.:*** Madopark; ***Switz.:*** Madopar; ***Thai.:*** Cenparkin†; Madopar; Vopar; ***Turk.:*** Madopar; ***UK:*** Madopar; ***Venez.:*** Madopar.