Levomepromazine Maleate *(BANM, USAN, rINNM)*

Levomepromatsiinimaleaatti; Levomepromazin maleinát; Lévomépromazine, maléate de; Levomepromazini maleas; Levomepromazinmaleat; Levomepromazin-maleát; Levomepromazino maleatas; Lewomepromazyny maleinian; Maleato de levomepromazina; Methotrimeprazine Hydrogen Maleate; Methotrimeprazine Maleate.

Левомепромазина Малеат

$C_{19}H_{24}N_2OS,C_4H_4O_4$ = 444.5.

CAS — 7104-38-3.

ATC — N05AA02.

ATC Vet — QN05AA02.

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

Ph. Eur. 6.2 (Levomepromazine Maleate). A white or slightly yellowish crystalline powder. It deteriorates when exposed to air and light. Slightly soluble in water and in alcohol; sparingly soluble in dichloromethane. The supernatant of a 2% dispersion in water has a pH of 3.5 to 5.5. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969, although it may be more sedating. See also Adverse Effects of Antihistamines, p.561.

Levomepromazine may cause severe orthostatic hypotension, and patients taking large initial doses, patients over 50 years of age, or those given injections, should be lying down. Children are very susceptible to the hypotensive and sedative effects of levomepromazine.

Interactions

As for Chlorpromazine, p.973.

Antidepressants. Although *MAOIs* have been used with phenothiazines without untoward effects, the use of levomepromazine with MAOIs should probably be avoided as this combination has been implicated in 2 fatalities.[1,2]

1. Barsa JA, Saunders JC. A comparative study of tranylcypromine and pargyline. *Psychopharmacologia* 1964; **6:** 295–8.
2. McQueen EG. New Zealand committee on adverse drug reactions: fourteenth annual report 1979. *N Z Med J* 1980; **91:** 226–9.

Pharmacokinetics

◊ In a study involving 5 psychiatric patients peak plasma concentrations of levomepromazine were noted 1 to 4 hours after oral doses and 30 to 90 minutes after injection into the gluteal muscle.[1] About 50% of an oral dose reached the systemic circulation. Although the metabolite levomepromazine sulfoxide could not be detected after a single intramuscular injection, it was found in concentrations higher than unmetabolised levomepromazine after single and multiple oral dosage, both substances reaching a steady state in the plasma within 7 days of starting multiple-dose oral therapy. Fluctuations in plasma concentration during multiple-dose oral therapy indicated that until the correlation between acute adverse effects and peak plasma concentration of levomepromazine had been further studied the total daily dose should be divided into 2 or 3 portions when larger oral doses of levomepromazine are used.

1. Dahl SG. Pharmacokinetics of methotrimeprazine after single and multiple doses. *Clin Pharmacol Ther* 1976; **19:** 435–42.

Half-life. In 8 psychiatric patients given levomepromazine 50 to 350 mg daily the plasma half-life showed wide variation, from 16.5 to 77.8 hours, and did not correlate with the dose given.[1]

1. Dahl SG, *et al.* Pharmacokinetics and relative bioavailability of levomepromazine after repeated administration of tablets and syrup. *Eur J Clin Pharmacol* 1977; **11:** 305–310.

Uses and Administration

Levomepromazine is a phenothiazine with pharmacological activity similar to that of both chlorpromazine (p.975) and promethazine (p.589). It has antihistaminic actions (p.561) as well as CNS effects resembling those of chlorpromazine. It is also reported to have analgesic activity. It is used in the treatment of various psychoses including schizophrenia (p.955), as an analgesic for moderate to severe pain usually in non-ambulatory patients, and for premedication (p.1780). It is also used in palliative care for the control of symptoms such as restlessness, agitation, and as an adjunct to opioid analgesia, as well as being an effective broad-spectrum antiemetic in nausea and vomiting (p.1700).

Levomepromazine is also used in veterinary medicine.

Levomepromazine is given orally as the maleate or the hydrochloride or by injection as the hydrochloride. In the UK, doses such as those given below are expressed in terms of the appropriate salt. However, in some countries, the dose of levomepromazine may be expressed in terms of the base. The embonate has also been used. Care is required in elderly patients because of the risk of severe hypotension; if levomepromazine is given to such patients reduced doses may be necessary.

The usual initial oral dose of levomepromazine maleate for the treatment of **schizophrenia** is 25 to 50 mg daily; the daily dosage is usually divided into 3 portions with a larger portion taken at night. Doses of 100 to 200 mg have been given to non-ambulant patients increased gradually up to 1 g daily if necessary. Children are very susceptible to the hypotensive and sedative effects of levomepromazine: a suggested oral dose for a 10-year-old is 12.5 to 25 mg of the maleate daily in divided doses; a dose of 37.5 mg daily should not be exceeded.

When used in **palliative care** as an adjunct to analgesics in the management of severe terminal **pain** and for the control of **nausea and vomiting**, levomepromazine maleate may be given orally in a dose of 12.5 to 50 mg every 4 to 8 hours. The *BNF* also includes an oral dose of levomepromazine maleate 6 to 25 mg daily given in 1 or 2 divided doses for the management of nausea and vomiting where first-line antiemetics have proved inadequate. Alternatively 12.5 to 25 mg of levomepromazine hydrochloride may be given intramuscularly every 6 to 8 hours but patients should remain in bed for at least the first few doses; doses of up to 50 mg have been given for severe agitation. Levomepromazine hydrochloride may also be given intravenously in similar doses after dilution with an equal volume of sodium chloride 0.9% injection. Alternatively it may be given, suitably diluted with sodium chloride 0.9% injection, by continuous subcutaneous infusion via a syringe driver; doses range from a total of 25 to 200 mg daily although lower doses of 5 to 25 mg daily may also be effective against nausea and vomiting. Experience with parenteral use of levomepromazine hydrochloride in children is limited but a dose of 100 to 400 micrograms/kg daily by continuous intravenous or subcutaneous infusion has been suggested for children aged 1 month and over in the management of nausea and vomiting in palliative care; it has also been used in the treatment of restlessness and confusion in palliative care in a dose of 0.35 to 3 mg/kg daily by continuous subcutaneous infusion in those aged 1 year and over.

Levomepromazine hydrochloride given intramuscularly has been used in some countries for the control of acute pain, as a **premedicant**, and for postoperative analgesia. In some countries levomepromazine is also licensed for use as an **anxiolytic** and **sedative**, and in the management of other types of pain, including **labour pain**.

Pain. As levomepromazine appears to possess intrinsic analgesic activity in addition to its antiemetic and antipsychotic actions it has been used for the symptomatic control of restlessness and vomiting and as an adjunct to opioid analgesics in pain control (see Choice of Analgesic, p.2) in terminally ill patients.

References.

1. Oliver DJ. The use of methotrimeprazine in terminal care. *Br J Clin Pract* 1985; **39:** 339–40.
2. Patt RB, *et al.* The neuroleptics as adjuvant analgesics. *J Pain Symptom Manage* 1994; **9:** 446–53.
3. O'Neill J, Fountain A. Levomepromazine (methotrimeprazine) and the last 48 hours. *Hosp Med* 1999; **60:** 564–7.
4. Skinner J, Skinner A. Levomepromazine for nausea and vomiting in advanced cancer. *Hosp Med* 1999; **60:** 568–70.

HEADACHE. Levomepromazine is one of those phenothiazines (see p.976) that has been effective[1] in relieving the pain of severe migraine attacks.

1. Stiell IG, *et al.* Methotrimeprazine versus meperidine and dimenhydrinate in the treatment of severe migraine: a randomized, controlled trial. *Ann Emerg Med* 1991; **20:** 1201–5.

Preparations

BP 2008: Levomepromazine Injection; Levomepromazine Tablets; ***USP 31:*** Methotrimeprazine Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Detenler; Levolam; Nozinan; Togrel; ***Austria:*** Nozinan; ***Belg.:*** Nozinan; ***Braz.:*** Levozine; Neozine; ***Canad.:*** Apo-Methoprazine; Novo-Mepraz ine†; Nozinan; ***Chile:*** Sinogan; ***Cz.:*** Tisercin; ***Denm.:*** Nozinan; ***Fin.:*** Levozin; Nozinan; ***Fr.:*** Nozinan; ***Ger.:*** Levium; Neurocil; ***Gr.:*** Nozinan; Prazine†; Sinogan; ***Hung.:*** Tisercin; ***Irl.:*** Nozinan; ***Israel:*** Methozane; Nozinan; Ronexine; ***Ital.:*** Nozinan; ***Mex.:*** Levocina; Sinogan; ***Neth.:*** Nozinan; ***Norw.:*** Nozinan; ***NZ:*** Nozinan; ***Philipp.:*** Nozinan; ***Pol.:*** Tisercin; ***Port.:*** Nozinan; ***Rus.:*** Tisercin (Тизерцин); ***Spain:*** Sinogan; ***Swed.:*** Nozinan; ***Switz.:*** Nozinan; ***UK:*** Levinan; Nozinan; ***Venez.:*** Sinogan.

Loprazolam Mesilate *(BANM, rINNM)*

HR-158; Loprazolam, Mésilate de; Loprazolam Mesylate; Loprazolam Methanesulphonate; Loprazolami Mesilas; Mesilato de loprazolam; RU-31158. 6-(2-Chlorophenyl)-2,4-dihydro-2-(4-methylpiperazin-1-ylmethylene)-8-nitroimidazo[1,2-*a*][1,4]benzodiazepin-1-one methanesulphonate monohydrate.

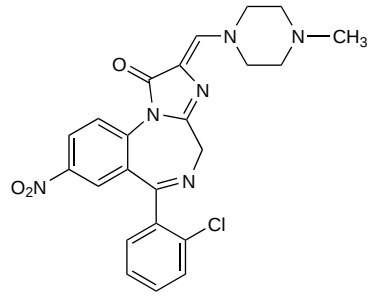
Лопразолама Мезилат

$C_{23}H_{21}ClN_6O_3,CH_4O_3S,H_2O$ = 579.0.

CAS — 61197-73-7 (loprazolam); 70111-54-5 (anhydrous loprazolam mesilate).

ATC — N05CD11.

ATC Vet — QN05CD11.



(loprazolam)

Pharmacopoeias. In *Br.*

BP 2008 (Loprazolam Mesilate). A yellow crystalline powder. Slightly soluble in water, in alcohol, and in chloroform; very slightly soluble in ether.

Dependence and Withdrawal

As for Diazepam, p.987.

◊ For the purpose of withdrawal regimens, 0.5 to 1 mg of loprazolam is considered equivalent to about 5 mg of diazepam.

Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987.

Porphyria. Loprazolam is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Interactions

As for Diazepam, p.989.

Pharmacokinetics

◊ References.

1. Garzone PD, Kroboth PD. Pharmacokinetics of the newer benzodiazepines. *Clin Pharmacokinet* 1989; **16:** 337–64.
2. Dorling MC, Hindmarch I. Pharmacokinetic profile of loprazolam in 12 young and 12 elderly healthy volunteers. *Drugs Exp Clin Res* 2001; **27:** 151–9.

Uses and Administration

Loprazolam is an intermediate-acting benzodiazepine with general properties similar to those of diazepam (p.992).

Loprazolam mesilate is usually used for its hypnotic properties in the short-term management of insomnia (p.957), in usual oral doses equivalent to 1 mg of loprazolam at night. Dosage may be increased to up to 2 mg if necessary. A starting dose of 0.5 mg increased to a maximum of 1 mg may be appropriate for elderly or debilitated patients.

Preparations

BP 2008: Loprazolam Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Dormonoct; ***Belg.:*** Dormonoct; ***Fr.:*** Havlane; ***Ger.:*** Sonin; ***Neth.:*** Dormonoct; ***Port.:*** Dormonoct; ***S.Afr.:*** Dormonoct; ***Spain:*** Somnovit.

Lorazepam *(BAN, USAN, rINN)*

Loratsepaami; Lorazépam; Lorazepám; Lorazepamas; Lorazepamum; Wy-4036. 7-Chloro-5-(2-chlorophenyl)-1,3-dihydro-3-hydroxy-1,4-benzodiazepin-2-one.

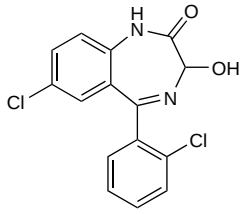
Лоразепам

$C_{15}H_{10}Cl_2N_2O_2$ = 321.2.

CAS — 846-49-1.

ATC — N05BA06.

ATC Vet — QN05BA06.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of lorazepam:
Benzo; Somnios.

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Lorazepam). A white or almost white, crystalline powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in alcohol; sparingly or slightly soluble in dichloromethane. Store in airtight containers. Protect from light.
USP 31 (Lorazepam). A white or practically white, practically odourless powder. Insoluble in water; sparingly soluble in alcohol; slightly soluble in chloroform. Store in airtight containers. Protect from light.

Incompatibility. Visual incompatibility has been noted with lorazepam and sargramostim[1] or aztreonam.[2]

1. Trissel LA, *et al.* Visual compatibility of sargramostim with selected antineoplastic agents, anti-infectives, or other drugs during simulated Y-site injection. *Am J Hosp Pharm* 1992; **49:** 402–6.
2. Trissel LA, Martinez JF. Compatibility of aztreonam with selected drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 1995; **52:** 1086–90.

Solubility. The solubility of lorazepam in fluids for intravenous use (water, glucose injection, lactated Ringer's injection, and sodium chloride injection) was greatest in glucose injection (5%) at 62 micrograms/mL and lowest in sodium chloride injection (0.9%) at 27 micrograms/mL;[1] these differences in solubility appeared to be pH related. Commercial injections are reported to contain polyethylene glycol in propylene glycol to overcome this poor solubility. However, precipitation has been noted[2] in solutions prepared by dilution of lorazepam injection with sodium chloride injection (0.9%) to a concentration of 500 micrograms/mL. One group of workers[3] have reported that they had overcome such problems with precipitation by using glucose injection (5%) as a diluent and by avoiding final concentrations of lorazepam between 0.08 mg/mL and 1 mg/mL. It was suggested that the propylene glycol in the mixture might account for the unusual concentration effect. Such recommendations have been adopted by another group[4] although they observed that precipitation occurred if a formulation of lorazepam containing 4 mg/mL was used to prepare the injection; no precipitation was noted when a formulation containing 2 mg/mL was used. The group also commented that, in the USA, licensed product information for lorazepam injection advises that admixtures should be prepared with the 2 mg/mL formulation only.

1. Newton DW, *et al.* Lorazepam solubility in and sorption from intravenous admixture solutions. *Am J Hosp Pharm* 1983; **40:** 424–7.
2. Boullata JI, *et al.* Precipitation of lorazepam infusion. *Ann Pharmacother* 1996; **30:** 1037–8.
3. Volles DF, *et al.* More on usability of lorazepam admixtures for continuous infusion. *Am J Health-Syst Pharm* 1996; **53:** 2753–4.
4. Levanda M. Noticeable difference in admixtures prepared from lorazepam 2 and 4 mg/ml. *Am J Health-Syst Pharm* 1998; **55:** 2305.

Sorption. Significant loss of lorazepam has been reported from solutions stored in PVC[1] or polypropylene[2] giving equipment; polyolefin[3-5] or glass[6] equipment appears to be more suitable.

1. Hoey LL, *et al.* Lorazepam stability in parenteral solutions for continuous intravenous administration. *Ann Pharmacother* 1996; **30:** 343–6.
2. Stiles ML, *et al.* Stability of deferoxamine mesylate, floxuridine, fluorouracil, hydromorphone hydrochloride, lorazepam, and midazolam hydrochloride in polypropylene infusion-pump syringes. *Am J Health-Syst Pharm* 1996; **53:** 1583–8.
3. Trissel LA, Pearson SD. Storage of lorazepam in three injectable solutions in polyvinyl chloride and polyolefin bags. *Am J Hosp Pharm* 1994; **51:** 368–72.
4. Norenberg JP, *et al.* Stability of lorazepam in 0.9% sodium chloride stored in polyolefin bags. *Am J Health-Syst Pharm* 2004; **61:** 1039–41.
5. Trissel LA, *et al.* Drug compatibility with new polyolefin infusion solution containers. *Am J Health-Syst Pharm* 2006; **63:** 2379–82.
6. Martens HJ, *et al.* Sorption of various drugs in polyvinyl chloride, glass, and polyethylene-lined infusion containers. *Am J Hosp Pharm* 1990; **47:** 369–73.

Dependence and Withdrawal

As for Diazepam, p.987.

◊ For the purpose of withdrawal regimens, 500 micrograms of lorazepam may be considered equivalent to about 5 mg of diazepam.

Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987. Pain and a sensation of burning have occurred following injection of lorazepam.

Breast feeding. The American Academy of Pediatrics[1] considers that, although the effect of lorazepam on breast-fed infants is unknown, its use by mothers during breast feeding may be of concern since anxiolytic drugs do appear in breast milk and thus could conceivably alter CNS function in the infant both in the short and long term.

Free lorazepam concentrations in the breast milk of 4 mothers ranged from 8 to 9 nanograms/mL four hours after receiving a 3.5-mg oral dose.[2] This represented about 15 to 26% of the concentration in plasma, and was probably sufficiently low to cause no adverse effects in breast-fed infants.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 28/04/04)
2. Summerfield RJ, Nielsen MS. Excretion of lorazepam into breast milk. *Br J Anaesth* 1985; **57:** 1042–3.

Effects on the blood. A case of pancytopenia associated with oral lorazepam was reported[1] in 1988; only 5 instances of thrombocytopenia and none of leucopenia had been reported to the UK CSM or the UK manufacturers over the previous 13 years.

1. El-Sayed S, Symonds RP. Lorazepam induced pancytopenia. *BMJ* 1988; **296:** 1332.

Effects on fluid and electrolyte homoeostasis. Inappropriate secretion of antidiuretic hormone related to ingestion of lorazepam was considered to be the cause of hyponatraemia in an 81-year-old woman.[1]

1. Engel WR, Grau A. Inappropriate secretion of antidiuretic hormone associated with lorazepam. *BMJ* 1988; **297:** 858.

Effects on the nervous system. For reference to extrapyramidal disorders associated with use of lorazepam, see Diazepam, p.988.

The elderly. For discussion of the need for reduced dosage of benzodiazepines in elderly patients, including mention of lorazepam, see Diazepam, p.989.

Formulation. There have been reports of toxicity, presumed to be due to polyethylene glycol[1,2] or propylene glycol,[3] after prolonged parenteral use of lorazepam; polyethylene glycol in propylene glycol is included as a solubiliser in lorazepam solutions. Diarrhoea in an infant given large enteral doses of lorazepam or diazepam solutions may have been due to the combined osmotic effect of polyethylene glycol and propylene glycol in these preparations.[4]

1. Laine GA, *et al.* Polyethylene glycol nephrotoxicity secondary to prolonged high-dose intravenous lorazepam. *Ann Pharmacother* 1995; **29:** 1110–4.
2. Tayar J *et al.* Severe hyperosmolar metabolic acidosis due to a large dose of intravenous lorazepam. *N Engl J Med* 2002; **346:** 1253–4.
3. Seay RE, *et al.* Possible toxicity from propylene glycol in lorazepam infusion. *Ann Pharmacother* 1997; **31:** 647–8. Woycik CL, Walker PC. Correction and comment: possible toxicity from propylene glycol in injectable drug preparations. *ibid.*: 1413.
4. Marshall JD, *et al.* Diarrhea associated with enteral benzodiazepine solutions. *J Pediatr* 1995; **126:** 657–9.

Hepatic impairment. Lorazepam is contra-indicated in severe hepatic impairment; patients with mild to moderate impairment may require reduced doses. Although the elimination half-life of lorazepam was increased in 13 patients with alcoholic cirrhosis compared with 11 control subjects, this was not associated with an impairment in systemic plasma clearance.[1] With the exception of a modest decrease in the extent of plasma protein binding, acute viral hepatitis had no effect on the disposition kinetics of lorazepam.

1. Kraus JW, *et al.* Effects of aging and liver disease on disposition of lorazepam. *Clin Pharmacol Ther* 1978; **24:** 411–19.

Local reactions. Of 40 patients given a single intravenous dose of lorazepam 4 mg three had local thrombosis 2 to 3 days later and 6 had local thrombosis 7 to 10 days later.[1] The incidence was lower than in those given diazepam [in solution].

1. Hegarty JE, Dundee JW. Sequelae after the intravenous injection of three benzodiazepines—diazepam, lorazepam, and flunitrazepam. *BMJ* 1977; **2:** 1384–5.

Interactions

As for Diazepam, p.989.

Pharmacokinetics

Lorazepam is readily absorbed from the gastrointestinal tract after oral doses, with a bioavailability of about 90%; peak plasma concentrations are reported to occur about 2 hours after an oral dose. The absorption profile after intramuscular injection is similar to that after oral dosage.

Lorazepam is about 85% bound to plasma proteins. It crosses the blood-brain barrier and the placenta; it is also distributed into breast milk. Lorazepam is metabolised in the liver to the inactive glucuronide, and excreted in urine. The elimination half-life has been reported to range from about 10 to 20 hours.

◊ References.

1. Greenblatt DJ. Clinical pharmacokinetics of oxazepam and lorazepam. *Clin Pharmacokinet* 1981; **6:** 89–105.
2. Swart EL, *et al.* Comparative population pharmacokinetics of lorazepam and midazolam during long-term continuous infusion in critically ill patients. *Br J Clin Pharmacol* 2004; **57:** 135–45.

Children. References to the pharmacokinetics of lorazepam in children.

1. Relling MV, *et al.* Lorazepam pharmacodynamics and pharmacokinetics in children. *J Pediatr* 1989; **114:** 641–6.

NEONATES. References to slow elimination of lorazepam by neonates.

1. Cummings AJ, Whitelaw AGL. A study of conjugation and drug elimination in the human neonate. *Br J Clin Pharmacol* 1981; **12:** 511–15.
2. McDermott CA, *et al.* Pharmacokinetics of lorazepam in critically ill neonates with seizures. *J Pediatr* 1992; **120:** 479–83.
3. Reiter PD, Stiles AD. Lorazepam toxicity in a premature infant. *Ann Pharmacother* 1993; **27:** 727–9.

Distribution. Evidence that lorazepam undergoes enterohepatic recirculation with possible first-pass metabolism.[1]

1. Herman RJ, *et al.* Disposition of lorazepam in human beings: enterohepatic recirculation and first-pass effect. *Clin Pharmacol Ther* 1989; **46:** 18–25.

CNS. In a study involving 6 healthy subjects, peak plasma-lorazepam concentrations were reached 5 minutes after the end of a one-minute intravenous injection.[1] CNS effects, as measured by EEG activity, were not maximal until 30 minutes after injection; they declined to baseline values slowly over 5 to 8 hours in a similar manner to plasma concentrations. In contrast, CNS effects of diazepam were maximal immediately after the injection. They also declined more rapidly than lorazepam, but again in a similar way to plasma concentrations. Studies in *mice* suggested that the slow onset of action of lorazepam that has been reported by some is at least partly explained by a delay in passage from systemic blood into brain tissue.

1. Greenblatt DJ, *et al.* Kinetic and dynamic study of intravenous lorazepam; comparison with intravenous diazepam. *J Pharmacol Exp Ther* 1989; **250:** 134–40.

Uses and Administration

Lorazepam is a short-acting benzodiazepine with general properties similar to those of diazepam (p.992). It is used in the short-term treatment of anxiety disorders (p.952), as a hypnotic in the short-term management of insomnia (p.957), and as an anticonvulsant in the management of status epilepticus (p.469). When used in the treatment of status epilepticus lorazepam has a prolonged antiepileptic action and may be the preferred initial treatment if intravenous access is available. It is also used for its sedative and amnestic properties in premedication and as an adjunct in regimens for the control of nausea and vomiting associated with cancer chemotherapy (p.1700).

Lorazepam is usually given orally or by injection as the base although the pivalate is available for oral use in some countries. Sublingual tablets are used in some countries in doses similar to those for standard tablets. The intramuscular route is usually only used when oral or intravenous dosage is not possible. Injections should usually be diluted before use; intravenous injections should be given at a rate of not more than 2 mg/minute into a large vein. Lorazepam should be given in reduced dosage to elderly or debilitated patients; half the usual adult dose, or less, may be sufficient.

The usual oral dose of lorazepam for the treatment of **anxiety disorders** is 1 to 6 mg daily in 2 or 3 divided doses with the largest dose taken at night; up to 10 mg daily has been given. A dose of 25 to