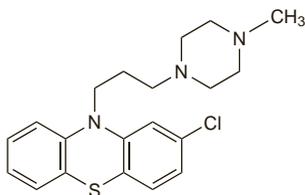


Prochlorperazine (BAN, rINN)

Chlormepazine; Prochlorpazine; Prochlorpérazine; Prochlorpazine; Prochlorperazina; Proklorperatsiini; Proklorperazin. 2-Chloro-10-[3-(4-methylpiperazin-1-yl)propyl]phenothiazine.

Прохлорперазин
 $C_{20}H_{24}ClN_3S = 373.9$.
 CAS — 58-38-8.
 ATC — N05AB04.
 ATC Vet — QN05AB04.



Pharmacopoeias. In US.

USP 31 (Prochlorperazine). A clear, pale yellow, viscous liquid, sensitive to light. Very slightly soluble in water; freely soluble in alcohol, in chloroform, and in ether. Store in airtight containers. Protect from light.

Prochlorperazine Edisilate (BANM, rINNM)

Chlormepazine Edisilate; Edisilato de prochlorperazina; Prochlorpazine Edisilate; Prochlorpérazine, Edisilate de; Prochlorperazine Edisilate; Prochlorperazine Ethanedisulphonate; Prochlorperazini Edisilas.

Прохлорперазина Эдизилат
 $C_{20}H_{24}ClN_3S_2 \cdot C_2H_6O_6S_2 = 564.1$.
 CAS — 1257-78-9.
 ATC — N05AB04.
 ATC Vet — QN05AB04.

Pharmacopoeias. In US.

USP 31 (Prochlorperazine Edisilate). A white to very light yellow odourless crystalline powder. Soluble 1 in 2 of water and 1 in 1500 of alcohol; insoluble in chloroform and in ether. Solutions in water are acid to litmus. Store in airtight containers. Protect from light.

Incompatibility. See under Prochlorperazine Mesilate, below.

Prochlorperazine Maleate (BANM, rINNM)

Chlormepazine Maleate; Maleato de prochlorperazina; Prochlorperazynny maleinian; Prochlorpazine Maleate; Prochlorperazine Dihydrogen Maleate; Prochlorperazine Dimaleate; Prochlorpérazine, Maléate de; Prochlorperazini maleas; Prochlorperazinmaleinát; Prochlorperazino maleatas; Proklorperatsiini maleaati; Proklorperazinmaleat; Proklorperazinmaleát.

Прохлорперазина Малейт
 $C_{20}H_{24}ClN_3S_2 \cdot C_4H_4O_4 = 606.1$.
 CAS — 84-02-6.
 ATC — N05AB04.
 ATC Vet — QN05AB04.

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

Ph. Eur. 6.2 (Prochlorperazine Maleate). A white or pale yellow, crystalline powder. Very slightly soluble in water and in alcohol. A freshly prepared saturated solution in water has a pH of 3.0 to 4.0. Protect from light.

USP 31 (Prochlorperazine Maleate). A white or pale yellow, practically odourless, crystalline powder. Practically insoluble in water; soluble 1 in 1200 of alcohol; slightly soluble in warm chloroform. Its saturated solution is acid to litmus. Store in airtight containers. Protect from light.

Prochlorperazine Mesilate (BANM, rINNM)

Chlormepazine Mesylate; Mesilato de prochlorperazina; Prochlorpazine Mesylate; Prochlorpérazine, mésilate de; Prochlorperazine Mesylate; Prochlorperazine Methanesulphonate; Prochlorperazini mesilas; Prochlorperazini Mesylas.

Прохлорперазина Мезилат
 $C_{20}H_{24}ClN_3S_2 \cdot CH_3SO_3H = 566.2$.
 CAS — 5132-55-8.
 ATC — N05AB04.
 ATC Vet — QN05AB04.

Pharmacopoeias. In Br.

BP 2008 (Prochlorperazine Mesilate). A white or almost white, odourless or almost odourless powder. Very soluble in water; sparingly soluble in alcohol; slightly soluble in chloroform; practically insoluble in ether. A 2% solution in water has a pH of 2.0 to 3.0. Protect from light.

Incompatibility. Incompatibility has been reported between the edisilate or mesilate salts of prochlorperazine and several other compounds; these include aminophylline, amphotericin B,

ampicillin sodium, aztreonam, some barbiturates, benzylpenicillin salts, calcium gluconate, cefalotin sodium, cefmetazole sodium, chloramphenicol sodium succinate, chlorothiazide sodium, dimenhydrinate, heparin sodium, hydrocortisone sodium succinate, midazolam hydrochloride, and some sulfonamides. Incompatibility between prochlorperazine edisilate and morphine sulfate has been attributed to phenol present in some formulations of the opioid.^{1,2} Incompatibility has been reported on dilution of prochlorperazine edisilate injection with sodium chloride injection containing methyl hydroxybenzoate and propyl hydroxybenzoate as preservatives.³ The problem did not occur with unpreserved sodium chloride or when benzyl alcohol was used as preservative. Prochlorperazine mesilate syrup has been reported to be incompatible with magnesium trisilicate mixture.⁴

1. Stevenson JG, Patriarca C. Incompatibility of morphine sulfate and prochlorperazine edisilate in syringes. *Am J Hosp Pharm* 1985; **42**: 2651.
2. Zuber DEL. Compatibility of morphine sulfate injection and prochlorperazine edisilate injection. *Am J Hosp Pharm* 1987; **44**: 67.
3. Jett S, et al. Prochlorperazine edisilate incompatibility. *Am J Hosp Pharm* 1983; **40**: 210.
4. Greig JR. Stemetil syrup and magnesium trisilicate. *Pharm J* 1986; **237**: 504.

Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969. Prochlorperazine may cause less sedation and fewer antimuscarinic effects but extrapyramidal effects may be more frequent.

Severe dystonic reactions have followed the use of prochlorperazine, particularly in children and adolescents. It should therefore be used with extreme care in children. In addition, in the UK, parenteral use in children is not recommended.

Local irritation has occurred after the use of buccal tablets of prochlorperazine maleate.

Effects on the cardiovascular system. Hypertension has been reported¹ in a few patients given prochlorperazine intravenously for prophylaxis of cisplatin-induced nausea and vomiting.

1. Roche H, et al. Hypertension and intravenous antidopaminergic drugs. *N Engl J Med* 1985; **312**: 1125-6.

Effects on the mouth. Reports of ulceration and soreness of the lip and tongue have been associated with use of prochlorperazine maleate oral tablets.^{1,2} The erosive cheilitis resolved after withdrawal of prochlorperazine and recurred on rechallenge.

1. Duxbury AJ, et al. Erosive cheilitis related to prochlorperazine maleate. *Br Dent J* 1982; **153**: 271-2.
2. Reilly GD, Wood ML. Prochlorperazine—an unusual cause of lip ulceration. *Acta Derm Venereol (Stockh)* 1984; **64**: 270-1.

Interactions

As for Chlorpromazine, p.973.

Pharmacokinetics

◇ The pharmacokinetics of prochlorperazine were studied in 8 healthy subjects after doses of 6.25 and 12.5 mg intravenously, and 25 mg by mouth.¹ There was a marked interindividual variation in pharmacokinetics after intravenous doses but no evidence of dose-dependent pharmacokinetics; mean terminal half-lives were 6.8 hours for the higher and 6.9 hours for the lower dose. The apparent volume of distribution was very high and plasma clearance values were apparently greater than liver plasma flow, suggesting that the liver may not be the only site of metabolism. After oral doses, prochlorperazine concentrations were detectable in only 4 of the 8 subjects, due in part to a low bioavailability but also to the lack of sensitivity of the high-pressure liquid chromatographic assay used. The time to peak plasma concentration varied from 1.5 to 5 hours, and the peak concentrations varied from 1.6 to 7.6 nanograms/mL. Bioavailability was estimated to range from 0 to 16%. A low bioavailability due to high first-pass metabolism would be expected because of the high plasma clearance of prochlorperazine.

1. Taylor WB, Bateman DN. Preliminary studies of the pharmacokinetics and pharmacodynamics of prochlorperazine in healthy volunteers. *Br J Clin Pharmacol* 1987; **23**: 137-42.

Buccal route. Both single- and multiple-dose studies indicated that bioavailability of prochlorperazine maleate was greater after buccal doses than when given orally.^{1,2} Doses of 3 mg twice daily by the buccal route and 5 mg three times daily by mouth produced similar steady-state plasma-prochlorperazine concentrations.¹

1. Hessell PG, et al. A comparison of the availability of prochlorperazine following im buccal and oral administration. *Int J Pharmaceutics* 1989; **52**: 159-64.
2. Finn A, et al. Bioavailability and metabolism of prochlorperazine administered via the buccal and oral delivery route. *J Clin Pharmacol* 2005; **45**: 1383-90.

Uses and Administration

Prochlorperazine is a phenothiazine antipsychotic with general properties similar to those of chlorpromazine

(p.975). It has a piperazine side-chain. Prochlorperazine and its salts are widely used in the prevention and treatment of nausea and vomiting (p.1700) including that associated with migraine or drug-induced emesis. They are also used for the short-term symptomatic relief of vertigo (p.565) as occurs in Ménière's disease (p.564) or labyrinthitis, and in the management of schizophrenia (p.955), mania (see Bipolar Disorder, p.372), and other psychoses. Prochlorperazine has been used as an adjunct in the short-term management of severe anxiety (p.952).

Prochlorperazine maleate is generally administered by the oral or buccal routes, while prochlorperazine edisilate and mesilate are given orally or parenterally. The base has been given rectally.

Depending on the country or the manufacturer, doses of prochlorperazine are expressed either as the base or the salt. Prochlorperazine edisilate 7.5 mg, prochlorperazine maleate 8.1 mg, or prochlorperazine mesilate 7.6 mg are equivalent to about 5 mg of prochlorperazine. Most doses in the UK are expressed in terms of the maleate or mesilate, while most doses in the USA are expressed in terms of the base. As a result there is a disparity in the dosage recommendations for these countries, with the doses in the USA tending to be higher.

Reduced dosage may be required in elderly patients.

For **nausea and vomiting** doses are as follows:

- in the UK, the usual *oral* dose for prevention is 5 to 10 mg of the maleate or mesilate (roughly equivalent to about 3 to 6.5 mg of the base) 2 or 3 times daily
- for the treatment of nausea and vomiting, recommended UK doses are 20 mg of the maleate or mesilate *orally* or 12.5 mg of the mesilate by deep *intramuscular* injection; further doses, preferably orally, are given if necessary. The recommended *buccal* dose of prochlorperazine maleate for this indication is 3 to 6 mg twice daily
- in the USA, the *oral* dose for the control of nausea and vomiting is the equivalent of 5 or 10 mg of the base (as edisilate or maleate) given 3 or 4 times daily; alternatively the equivalent of 10 mg of the base twice daily or 15 mg once daily of the base (both as the maleate) may be taken as modified-release capsules. The recommended *intramuscular* dosage is the equivalent of 5 to 10 mg of the base (as edisilate) given every 3 to 4 hours if necessary, up to a total of 40 mg of the base daily. The *rectal* dose is 25 mg of the base given twice daily. In the management of severe nausea and vomiting the equivalent of 2.5 to 10 mg of prochlorperazine (as the edisilate) may be given by slow *intravenous* injection or infusion at a rate not exceeding 5 mg/minute; doses should not exceed 40 mg daily

For treatment of **psychoses** the following doses have been given:

- in the UK, prochlorperazine maleate or mesilate may be given in an *oral* dose of 12.5 mg twice daily for 7 days adjusted gradually to 75 to 100 mg daily according to response; some patients may be maintained on doses of 25 to 50 mg daily. The equivalent of prochlorperazine mesilate 12.5 to 25 mg two or three times daily may be given by deep *intramuscular* injection
- in the USA, prochlorperazine is given as the maleate or edisilate in usual initial *oral* doses equivalent to 5 or 10 mg of the base 3 or 4 times daily adjusted according to response up to a maximum of 150 mg of base daily. In acute disturbances it may be given by deep *intramuscular* injection as the edisilate in doses equivalent to 10 to 20 mg of the base and repeated every 2 to 6 hours if necessary

There are similar discrepancies with **children's doses**. Owing to the risk of severe extrapyramidal reactions, prochlorperazine should be used with extreme caution in children; it is not recommended for very young children or those weighing less than 10 kg. Where use in