children is unavoidable, UK licensed product information has suggested that 250 micrograms/kg of the maleate or mesilate may be given orally 2 or 3 times daily to children aged 1 year and over for the prevention and treatment of nausea and vomiting; the intramuscular route is considered unsuitable. However, the *BNFC* suggests giving intramuscular doses, repeated up to 3 times daily if necessary, according to age as follows: 2 to 5 years, 1.25 to 2.5 mg; 5 to 12 years, 5 to 6.25 mg.

In the USA oral, rectal, and intramuscular routes have all been advocated for children aged 2 years and over. The usual oral or rectal antiemetic dose ranges up to 7.5 mg of the base or its equivalent daily in children weighing 10 to 13 kg; in children 14 to 17 kg, up to 10 mg daily; from 18 to 39 kg, up to 15 mg daily. Higher doses have been given for psychoses. The suggested intramuscular dose for children in the USA is the equivalent of about 130 micrograms/kg of base given as a single deep intramuscular injection of the edisilate.

Oral doses of 5 to 10 mg of the maleate or mesilate (or, in the USA, the equivalent of 5 mg of the base) up to 3 or 4 times daily have been used for short-term adjunctive management of **severe anxiety disorders**. A modified-release preparation may be given in doses similar to those used in nausea and vomiting.

Prochlorperazine is also used in the UK in the treatment of **vertigo** including that due to Ménière's disease. It is given *orally* in doses of 15 to 30 mg of the maleate or mesilate daily in divided doses; after several weeks the dose may be gradually reduced to 5 to 10 mg daily. The recommended *buccal* dose of prochlorperazine maleate for this indication is 3 to 6 mg twice daily.

Headache. Some phenothiazines such as prochlorperazine have been used in the control of the symptoms of severe migraine (see p.976). In comparative studies[1,2] prochlorperazine appears to have been more effective in relieving migraine headache and nausea and vomiting than metoclopramide when these drugs were given parenterally. Intravenous prochlorperazine was shown to be effective in aborting intractable migraine in children in a small uncontrolled study.[3]

1. Coppola M, *et al.* Randomized, placebo-controlled evaluation of prochlorperazine versus metoclopramide for emergency department treatment of migraine headache. *Ann Emerg Med* 1995; **26:** 541–6.
2. Jones J, *et al.* Intramuscular prochlorperazine versus metoclopramide as single-agent therapy for the treatment of acute migraine headache. *Am J Emerg Med* 1996; **14:** 262–4.
3. Kabbouche MA, *et al.* Tolerability and effectiveness of prochlorperazine for intractable migraine in children. *Pediatrics* 2001; **107:** 767. Full version: http://pediatrics.aappublications.org/cgi/content/full/107/4/e62 (accessed 28/04/04)

Preparations

BP 2008: Prochlorperazine Buccal Tablets; Prochlorperazine Injection; Prochlorperazine Oral Solution; Prochlorperazine Tablets;
USP 31: Prochlorperazine Edisylate Injection; Prochlorperazine Maleate Tablets; Prochlorperazine Oral Solution; Prochlorperazine Suppositories.

Proprietary Preparations (details are given in Part 3)

Austral.: Stemetil; Stemzine; ***Canad.:*** Apo-Prochlorazine; Nu-Prochlor; Stemetil; ***Denm.:*** Stemetil; ***Fin.:*** Stemetil; ***Hong Kong:*** Dhaperazine; Seratil; Stemetil; ***India:*** Bukatel†; Emidoxyn; Stemetil; Vometil; ***Irl.:*** Buccastem; Stemetil; ***Ital.:*** Stemetil; ***Malaysia:*** Dhaperazine; Nautisol; Prochlor; Stemetil†; ***Neth.:*** Stemetil; ***Norw.:*** Stemetil; ***NZ:*** Antinaus; Buccastem; Stemetil; ***Pol.:*** Chloropernazinum; ***S.Afr.:*** Mitil; Scripto-Metic; Stemetil; ***Singapore:*** Dhaperazine; Prochlor; Stemetil; ***Swed.:*** Stemetil; ***Thai.:*** Proclozine; Stemetil; ***UK:*** Buccastem; Prozieret; Stemetil; ***USA:*** Compazine; Compro.

Multi-ingredient: ***Ital.:*** Difmetre.

Promazine *(BAN, rINN)*

A-145; NSC-31447; Promatsiini; Promazin; Promazina; Promazinum; Propazinum; 3276-RP; RP-3276; WY-1094. *NN*-Dimethyl-3-phenothiazin-10-ylpropylamine.

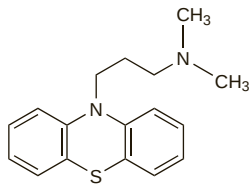
Промазин

$C_{17}H_{20}N_2S$ = 284.4.

CAS — 58-40-2.

ATC — N05AA03.

ATC Vet — QN05AA03.



NOTE. The code A-145 has also been used for *N*-ethylcarbaminomethyl-*L*-isoleucine, a compound investigated as an antineoplastic

Promazine Embonate *(BANM, rINNM)*

Embonato de promazina; Promazine, Embonate de; Promazine Pamoate; Promazini Embonas.

Промазина Эмбонат

$(C_{17}H_{20}N_2S)_2,C_{23}H_{16}O_6$ = 957.2.

ATC — N05AA03.

ATC Vet — QN05AA03.

Promazine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de promazina; Promatsiinihydrokloridi; Promazine, chlorhydrate de; Promazin-hidroklorid; Promazin-hydrochlorid; Promazinhydroklorid; Promazini hydrochloridum; Promazino hidrochloridas; Promazyny chlorowodorek.

Промазина Гидрохлорид

$C_{17}H_{20}N_2S$,HCl = 320.9.

CAS — 53-60-1.

ATC — N05AA03.

ATC Vet — QN05AA03.

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

Ph. Eur. 6.2 (Promazine Hydrochloride). A white or almost white, slightly hygroscopic, crystalline powder. Very soluble in water, in alcohol, and in dichloromethane. A freshly prepared 5% solution in water has a pH of 4.2 to 5.2. Protect from light.

USP 31 (Promazine Hydrochloride). A white or slightly yellow, practically odourless, crystalline powder. It oxidises upon prolonged exposure to air and acquires a pink or blue colour. Soluble 1 in 3 of water; freely soluble in chloroform. pH of a 1 in 20 solution is between 4.2 and 5.2. Store in airtight containers. Protect from light.

Incompatibility. Incompatibility has been reported between promazine hydrochloride and several other compounds: these include aminophylline, some barbiturates, benzylpenicillin potassium, chlortetracycline, chlorothiazide sodium, dimenhydrinate, heparin sodium, hydrocortisone sodium succinate, phenytoin sodium, prednisolone sodium phosphate, and sodium bicarbonate.

Sorption. A study[1] of drug loss from intravenous delivery systems reported an 11% loss of promazine hydrochloride from solution when infused for 7 hours via a plastic infusion set, and a 59% loss after infusion for one hour from a glass syringe through silastic tubing. Loss was negligible after infusion for 1 hour from a system comprising a glass syringe with polyethylene tubing.

1. Kowaluk EA, *et al.* Interactions between drugs and intravenous delivery systems. *Am J Hosp Pharm* 1982; **39:** 460–7.

Stability. A study of the stability of promazine diluted to a 0.1% infusion in sodium chloride 0.9% or glucose 5% found that solutions in glucose 5% remained stable for up to 6 days at 4°, and at room temperature, provided they were stored in the dark.[1] However, with sodium chloride 0.9% as the diluent, deterioration of promazine was observed 24 hours after preparation, even when stored in the dark, and after 8 hours when exposed to light. Temperature had no effect on degradation rate.

1. Tebbett IR, *et al.* Stability of promazine as an intravenous infusion. *Pharm J* 1986; **237:** 172–4.

Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969.

Pregnancy. An increased incidence of neonatal jaundice coincided with the increased use of promazine.[1] A decrease in the incidence of jaundice was noted 3 months after the total withdrawal of the drug from the hospital although restriction of its use during labour had no impact.

1. John E. Promazine and neonatal hyperbilirubinaemia. *Med J Aust* 1975; **2:** 342–4.

Interactions

As for Chlorpromazine, p.973.

Pharmacokinetics

The pharmacokinetics of promazine appear to be generally similar to those of chlorpromazine (p.975).

Uses and Administration

Promazine is a phenothiazine with general properties similar to those of chlorpromazine (p.975). It has relatively weak antipsychotic activity and is not generally used for the management of psychoses. It is mainly used for the short-term management of agitated or disturbed behaviour (p.954). It has also been given for the alleviation of nausea and vomiting (p.1700). Promazine is given as the hydrochloride by mouth, intramuscularly, or by slow intravenous injection. Promazine has also been given by mouth as the embonate.

For the treatment of **agitated behaviour**, promazine is given in doses equivalent to 100 to 200 mg of the hydrochloride 4 times daily by mouth or 50 mg by intramuscular injection repeated if necessary after 6 to 8 hours. It has also been given by slow intravenous injection in concentrations not exceeding 25 mg/mL, for severely agitated hospitalised patients.

An oral dose of 25 to 50 mg every 4 to 6 hours has been given for the control of **nausea and vomiting**; it has also been given by intramuscular injection for this indication.

Promazine should be given in reduced dosage to elderly or debilitated patients; 25 mg orally of the hydrochloride initially, increasing, if necessary, to 50 mg four times daily has been suggested for the control of agitation and restlessness; for intramuscular injection, a dose of 25 mg may be sufficient.

Hiccup. Promazine hydrochloride has been used in some countries for the treatment of intractable hiccup. A protocol for the management of intractable hiccups may be found under Chlorpromazine, p.976.

Preparations

BP 2008: Promazine Injection; Promazine Tablets;
USP 31: Promazine Hydrochloride Injection; Promazine Hydrochloride Oral Solution; Promazine Hydrochloride Syrup; Promazine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Belg.: Prazine†; ***Denm.:*** Sparine†; ***Fin.:*** Sparine†; ***Ger.:*** Protactyl†; Sinophenin†; ***Gr.:*** Sinophenin; Sparine†; ***Ital.:*** Talofen; ***S.Afr.:*** Sparine; ***Switz.:*** Prazine; ***USA:*** Prozine.

Propionylpromazine

Dipropimazine; Propionilpromazina; Propiopromazine.

CAS — 3568-24-9.

Profile

Propionylpromazine is a phenothiazine antipsychotic that has been used for sedation and premedication in veterinary medicine.

Prothipendyl Hydrochloride *(BANM, rINNM)*

D-206; Hidrocloruro de protipendilo; Phrenotropin; Prothipendyl, Chlorhydrate de; Prothipendyli Hydrochloridum. *NN*-Dimethyl-3-(pyrido[3,2-*b*][1,4]benzothiazin-10-yl)propylamine hydrochloride monohydrate.

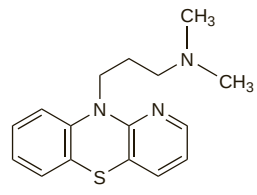
Протипендила Гидрохлорид

$C_{16}H_{19}N_3S$,HCl,H_2O = 339.9.

CAS — 303-69-5 (prothipendyl); 1225-65-6 (anhydrous prothipendyl hydrochloride).

ATC — N05AX07.

ATC Vet — QN05AX07.



(prothipendyl)

Profile

Prothipendyl is an azaphenothiazine with general properties similar to those of chlorpromazine (p.969). It is given as the hydrochloride in oral doses of 40 to 80 mg two to four times daily for the treatment of psychoses and agitation, and as an adjunct to analgesics in the treatment of severe pain. Prothipendyl hydrochloride may also be given by injection.

Preparations

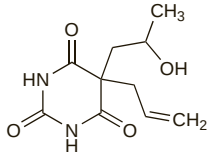
Proprietary Preparations (details are given in Part 3)
Austria: Dominal; ***Belg.:*** Dominal; ***Ger.:*** Dominal.

Proxibarbal *(rINN)*

HH-184; Proksybarbal; Proxibarbalum; Proxibarbital. 5-Allyl-5-(2-hydroxypropyl)barbituric acid.

Проксибарбал

$C_{10}H_{14}N_2O_4$ = 226.2.
CAS — 2537-29-3.
ATC — N05CA22.
ATC Vet — QN05CA22.



Pharmacopoeias. In *Pol.*

Profile
Proxibarbal is a barbiturate with general properties similar to those of amobarbital (p.961). It has been used as a sedative in the management of anxiety disorders. It has also been used in the treatment of headache. However, barbiturates are not considered appropriate in the management of these conditions. Proxibarbal has been associated with severe hypersensitivity-induced thrombocytopenia.

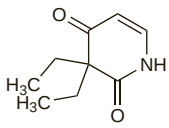
Preparations
Proprietary Preparations (details are given in Part 3)
Hung.: Vasalgin.

Pyrithyldione *(rINN)*

Didropyridinum; NU-903; Piritildiona; Pyrithyldionum; Pyrityldion; Pyrityylidioni. 3,3-Diethylpyridine-2,4(1*H*,3*H*)-dione.

Пиритильдион

$C_9H_{13}NO_2$ = 167.2.
CAS — 77-04-3.
ATC — N05CE03.
ATC Vet — QN05CE03.



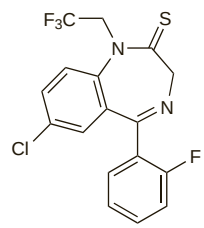
Profile
Pyrithyldione has been given in preparations with diphenhydramine in the short-term management of insomnia but there have been reports of agranulocytosis associated with the use of this combination.

Quazepam *(BAN, USAN, rINN)*

Kvatsepaami; Kvazepam; Quazépam; Quazepamum; Sch-16134. 7-Chloro-5-(2-fluorophenyl)-1,3-dihydro-1-(2,2,2-trifluoroethyl)-1,4-benzodiazepine-2-thione.

Квазепам

$C_{17}H_{11}ClF_4N_2S$ = 386.8.
CAS — 36735-22-5.
ATC — N05CD10.
ATC Vet — QN05CD10.



Pharmacopoeias. In *US.*
USP 31 (Quazepam). Off-white to yellowish powder.

Dependence and Withdrawal
As for Diazepam, p.987.

Adverse Effects, Treatment, and Precautions
As for Diazepam, p.987.

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

However, a study in 4 women given a single 15-mg dose of quazepam found that only about 0.1% of the dose was excreted over 48 hours in breast milk, as quazepam and its 2 major metabolites.[2]

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. Hilbert JM, *et al.* Excretion of quazepam into human breast milk. *J Clin Pharmacol* 1984; **24:** 457–62.

Interactions
As for Diazepam, p.989.

Pharmacokinetics
Quazepam is readily absorbed from the gastrointestinal tract after oral doses, peak plasma concentrations being reached in about 2 hours. It is metabolised extensively in the liver. The principal active metabolites are 2-oxoquazepam and *N*-desalkyl-2-oxoquazepam (*N*-desalkylflurazepam) which have elimination half-lives of about 39 and 73 hours respectively, compared with a half-life of 39 hours for quazepam. Further hydroxylation occurs and quazepam is excreted in urine and faeces mainly as conjugated metabolites.

Quazepam and its two active metabolites are more than 95% bound to plasma proteins. Quazepam and its metabolites are distributed into breast milk.

Uses and Administration
Quazepam is a long-acting benzodiazepine with general properties similar to those of diazepam (p.992). It is given as a hypnotic in the short-term management of insomnia (p.957), in an initial oral dose of 15 mg at night; in elderly or debilitated patients and some other patients this can be reduced to 7.5 mg.

Preparations
USP 31: Quazepam Tablets.

Proprietary Preparations (details are given in Part 3)
Ital.: Quazium†; ***Jpn:*** Doral; ***Port.:*** Prosedar†; ***S.Afr.:*** Dorme†; ***Spain:*** Quiedorm; ***USA:*** Doral.

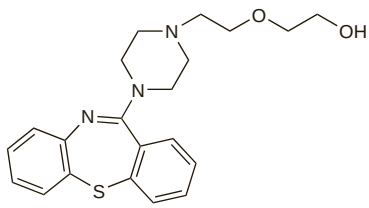
Quetiapine Fumarate

(BANM, USAN, pINNM)

Fumarato de quetiapina; ICI-204636; Quétiapine, Fumarate de; Quetiapini Fumaras; ZD-5077; ZM-204636. 2-[2-(4-Dibenzo[*b*,*f*][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]ethanol fumarate (2:1) salt.

Кветиапина Фумарат

$(C_{21}H_{25}N_3O_2S)_2, C_4H_4O_4$ = 883.1.
CAS — 111974-69-7 (quetiapine); 111974-72-2 (quetiapine fumarate).
ATC — N05AH04.
ATC Vet — QN05AH04.



(quetiapine)

Adverse Effects, Treatment, and Precautions
Although quetiapine may share some of the adverse effects seen with the classical antipsychotics (see Chlorpromazine, p.969), the incidence and severity of such effects may vary. Quetiapine has been associated with a low incidence of extrapyramidal symptoms but tardive dyskinesia may occur after long-term treatment. Rises in prolactin concentrations may be less than with chlorpromazine.

The most frequent adverse effects with quetiapine are somnolence and dizziness. Mild asthenia, anxiety, fever, rhinitis, peripheral oedema, constipation, dyspepsia, dry mouth, and raised liver enzyme values are also relatively common. Orthostatic hypotension associated with dizziness, tachycardia, and syncope has been reported, particularly during initial dose-titration. Prolongation of QT interval is rarely significant with quetiapine. Hyperglycaemia and exacerbation of pre-existing diabetes have been reported rarely. Clinical monitoring for hyperglycaemia has been recommended, especially in patients with, or at risk of developing, diabetes. Weight gain, particularly during early treatment, has also been noted. Neuroleptic malignant syndrome is rare with quetiapine. Leucopenia, neutropenia, and eosinophilia have also been reported. Other adverse effects have included rises in plasma-triglyceride and cholesterol concentrations, and reduced plasma-thyroid hormone concentrations. There have been rare reports of seizures, hypersensitivity reactions including angioedema, and priapism.

Asymptomatic changes in the lens of the eye have occurred in patients during long-term treatment with quetiapine; cataracts have developed in *dogs* during chronic dosing studies. In the USA, it is recommended that patients should have an eye examination to detect cataract formation when starting therapy with quetiapine and every 6 months during treatment.

Quetiapine should be used with caution in patients with hepatic or renal impairment, with cardiovascular disease or other conditions predisposing to hypotension, with cerebrovascular disease, or with a history of seizures or conditions that lower the seizure threshold.

When quetiapine is used for the depressive phase in bipolar disorder, patients should be closely monitored during early therapy until significant improvement in depression is observed because suicide is an inherent risk in depressed patients. For further details, see under Bipolar Disorder, p.372.

Quetiapine may affect the performance of skilled tasks including driving.

Gradual withdrawal of quetiapine is recommended because of the risk of withdrawal symptoms, including nausea, vomiting, insomnia, and rebound psychoses, with abrupt cessation.

Breast feeding. In a case report[1] of a mother receiving quetiapine 200 mg daily by mouth, the maximum concentration of the drug in breast milk an hour after the dose was reported to be 62 micrograms/litre; the mean concentration over 6 hours was 13 micrograms/litre. The authors concluded that the breast-fed infant would ingest, at maximum, the daily equivalent of 0.43% of the weight-adjusted maternal dose. Follow-up at 4.5 months reported no adverse effects in the infant, who had been breast fed from 8 weeks of age.

Licensed product information recommends that patients receiving quetiapine should not breast feed.

1. Lee A, *et al.* Excretion of quetiapine in breast milk. *Am J Psychiatry* 2004; **161:** 1715–16.

Dementia. The FDA[1] has issued advice against the use of atypical antipsychotics in the treatment of behavioural problems in elderly patients with dementia after analysis of placebo-controlled studies showed an increased risk of mortality with certain drugs of this class, including quetiapine; most of the deaths appeared due to cardiovascular events or infection. See also under Risperidone, p.1024.

1. FDA. FDA issues public health advisory for antipsychotic drugs used for treatment of behavioral disorders in elderly patients (issued 11th April, 2005). Available at: http://www.fda.gov/bbs/topics/ANSWERS/2005/ANS01350.html (accessed 30/05/05)

Effects on the blood. There have been reports of leucopenia,[1] neutropenia,[2] and pancytopenia[3] associated with quetiapine therapy; all 3 patients improved when the drug was stopped. Thrombotic thrombocytopenic purpura has also been reported in a patient who received quetiapine on 2 separate occasions 2 years apart.[4] From December 1997 to October 2006, Health Canada[5] had received 11 reports of thrombocytopenia associated with quetiapine, 6 of which were associated with quetiapine alone. In one of these 6 cases, thrombocytopenia recurred 3 months after restarting quetiapine, which had stopped for 1 month.

1. Clark N, *et al.* Quetiapine and leukopenia. *Am J Psychiatry* 2001; **158:** 817–18.
2. Croarkin P, Rayner T. Acute neutropenia in a patient treated with quetiapine. *Psychosomatics* 2001; **42:** 368.
3. Iraqi A. A case report of pancytopenia with quetiapine use. *Am J Geriatr Psychiatry* 2003; **11:** 694.
4. Huynh M, *et al.* Thrombotic thrombocytopenic purpura associated with quetiapine. *Ann Pharmacother* 2005; **39:** 1346–8.
5. Health Canada. Quetiapine: pancreatitis and thrombocytopenia. *Can Adverse React News* 2007; **17** (2): 1–2. Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/carn-bcei_v17n2_e.pdf (accessed 09/04/08)