ability. Giving an antacid could reverse this effect. Renal failure had no other effect on the pharmacokinetics of triazolam which could probably be given in usual doses.

1. Kroboth PD, *et al.* Effects of end stage renal disease and aluminium hydroxide on triazolam pharmacokinetics. *Br J Clin Pharmacol* 1985; **19:** 839–42.

Interactions
As for Diazepam, p.989.

Pharmacokinetics
Triazolam is rapidly and nearly completely absorbed from the gastrointestinal tract, peak plasma concentrations being achieved within 2 hours of an oral dose. Triazolam has a plasma elimination half-life ranging from 1.5 to 5.5 hours. It is reported to be about 89% bound to plasma proteins. Hydroxylation of triazolam in the liver is mediated by the cytochrome P450 isoenzyme CYP3A4. Triazolam is excreted in the urine mainly in the form of its conjugated metabolites with only small amounts appearing unchanged.

◊ References.

1. Garzone PD, Kroboth PD. Pharmacokinetics of the newer benzodiazepines. *Clin Pharmacokinet* 1989; **16:** 337–64.
2. Greenblatt DJ, *et al.* Age and gender effects on the pharmacokinetics and pharmacodynamics of triazolam, a cytochrome P450 3A substrate. *Clin Pharmacol Ther* 2004; **76:** 467–79.

Uses and Administration
Triazolam is a short-acting benzodiazepine with general properties similar to those of diazepam (p.992). It is used as a hypnotic in the short-term management of insomnia (p.957) in oral doses of 125 to 250 micrograms at night for no more than 2 weeks; doses of up to 500 micrograms at night have been used for resistant cases but these may be associated with an increased risk of severe adverse effects (see Effects on Mental Function, above). Initial doses of 125 micrograms at night have been suggested for elderly or debilitated subjects, increased up to a maximum of 250 micrograms only if necessary.

Administration in hepatic or renal impairment. See under Precautions, above.

Preparations
USP 31: Triazolam Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Halcion; ***Austria:*** Halcion; ***Belg.:*** Halcion; ***Braz.:*** Halcion†; ***Canad.:*** Apo-Triazo; Halcion; ***Chile:*** Balidon; Somese; ***Cz.:*** Halcion†; ***Denm.:*** Halcion; Rilamir; ***Fin.:*** Halcion; ***Fr.:*** Halcion†; ***Ger.:*** Halcion; ***Gr.:*** Halcion; ***Hong Kong:*** Halcion; ***Irl.:*** Halcion; Trilam; ***Israel:*** Halcion; ***Ital.:*** Halcion; Songar; ***Malaysia:*** Somese; ***Mex.:*** Halcion; ***Neth.:*** Halcion†; ***NZ:*** Halcion; Hypam; ***Port.:*** Halcion; ***S.Afr.:*** Halcion; ***Spain:*** Halcion; ***Swed.:*** Halcion; ***Switz.:*** Halcion; ***Thai.:*** Halcion; Trycam†; ***USA:*** Halcion; ***Venez.:*** Somese.

Triclofos Sodium *(BANM, USAN, rINNM)*

Natrii Triclofosum; Sch-10159; Sodium Triclofos; Triclofós sódico; Triclofos Sodique. Sodium 2,2,2-trichloroethyl hydrogen orthophosphate.

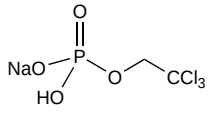
Натрий Триклофос

$C_2H_3Cl_3NaO_4P$ = 251.4.

CAS — 306-52-5 (triclofos); 7246-20-0 (triclofos sodium).

ATC — N05CM07.

ATC Vet — QN05CM07.



Pharmacopoeias. In *Br.* and *Jpn.*
BP 2008 (Triclofos Sodium). A white or almost white, odourless or almost odourless, hygroscopic powder. Freely soluble in water; slightly soluble in alcohol; practically insoluble in ether. A 2% solution in water has a pH of 3.0 to 4.5.

Dependence and Withdrawal, Adverse Effects, Treatment, and Precautions
As for Cloral Hydrate, p.979 but causes fewer gastrointestinal disturbances. Also, triclofos sodium is not corrosive to skin and mucous membranes.

Interactions
As for Cloral Hydrate, p.979.

Pharmacokinetics
Triclofos sodium is rapidly hydrolysed to trichloroethanol, peak serum concentrations being achieved within about one hour after oral dosage. For the pharmacokinetics of trichloroethanol, see Cloral Hydrate, p.979.

Uses and Administration
Triclofos sodium has hypnotic and sedative actions similar to those of cloral hydrate (p.979) but it is more palatable and causes less gastric irritation. It is used similarly in the short-term management of insomnia (p.957) and for sedation of children before painless procedures; however, its use as a hypnotic, particularly in children, is now limited.

The usual adult dose as a hypnotic is 1 to 2 g orally at night. A suggested hypnotic dose for children 1 month to 1 year of age is 25 to 30 mg/kg; children aged 1 to 5 years may be given single doses of 250 to 500 mg, and children aged 6 to 12 years may be given single doses of 0.5 to 1 g. Although not licensed in the UK for sedation of children before painless procedures, the *BNFC* suggests that those aged 1 month to 18 years may be given 30 to 50 mg/kg (maximum of 2 g) 45 to 60 minutes before the procedure; up to 100 mg/kg (maximum of 2 g) may be used with respiratory monitoring.

Preparations
BP 2008: Triclofos Oral Solution.

Proprietary Preparations (details are given in Part 3)
India: Tricloryl; ***Irl.:*** Tricloryl†; ***Israel:*** Triclonam.

Trifluoperazine Hydrochloride

(BANM, rINNM)

Hidrocloruro de trifluoperazina; Trifluoperazin Hidroklorür; Trifluoperazin hydrochlorid; Trifluopérazine, chlorhydrate de; Trifluoperazinhidroklorid; Trifluoperazinhydroklorid; Trifluoperazini hydrochloridum; Trifluoperazino hidrochloridas; Trifluoperazyny chlorowodorek; Trifluoriperatsiinihydrokloridi; Triphthazinum. 10-[3-(4-Methylpiperazin-1-yl)propyl]-2-trifluoromethylphenothiazine dihydrochloride.

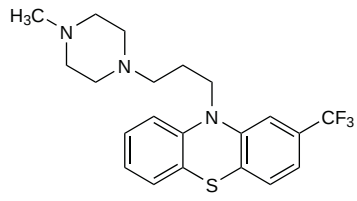
Трифлуоперазина Гидрохлорид

$C_{21}H_{24}F_3N_3S,2HCl$ = 480.4.

CAS — 117-89-5 (trifluoperazine); 440-17-5 (trifluoperazine hydrochloride).

ATC — N05AB06.

ATC Vet — QN05AB06.



(trifluoperazine)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US.*
Ph. Eur. 6.2 (Trifluoperazine Hydrochloride). A white to pale yellow, hygroscopic, crystalline powder. Freely soluble in water; soluble in alcohol; practically insoluble in ether. A 10% solution in water has a pH of 1.6 to 2.5. Protect from light.
USP 31 (Trifluoperazine Hydrochloride). A white to pale yellow, practically odourless, crystalline powder. Soluble 1 in 3.5 of water, 1 in 11 of alcohol, and 1 in 100 of chloroform; insoluble in ether and in benzene. pH of a 1 in 20 solution is between 1.7 and 2.6. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Adverse Effects, Treatment, and Precautions
As for Chlorpromazine, p.969. Trifluoperazine is less likely to cause sedation, hypotension, hypothermia, or antimuscarinic effects but is associated with a higher incidence of extrapyramidal effects particularly when the daily dose exceeds 6 mg.

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

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 29/04/04)

Interactions
As for Chlorpromazine, p.973.

Pharmacokinetics
Trifluoperazine hydrochloride is readily absorbed from the gastrointestinal tract after oral doses; peak plasma concentrations are attained 1.5 to 6 hours after ingestion and bioavailability is subject to interindividual variation. It is highly bound to plasma proteins. The elimination of trifluoperazine is multiphasic and the terminal half-life is about 22 hours. The major metabolite is the possibly active *N*-oxide. Other metabolites include the sulfoxide and the 7-hydroxy derivative. Trifluoperazine is distributed into breast milk.

Uses and Administration
Trifluoperazine is a phenothiazine antipsychotic with general properties similar to those of chlorpromazine (p.975). It has a piperazine side-chain.

Trifluoperazine is used in the treatment of a variety of psychiatric disorders including schizophrenia (p.955), severe anxiety (p.952), and disturbed behaviour (p.954). It is also used for the control of nausea and vomiting (p.1700).

Trifluoperazine is given as the hydrochloride but doses are expressed in terms of the base. Trifluoperazine 1 mg is equivalent to about 1.2 mg of trifluoperazine hydrochloride. A modified-release preparation is also available in some countries. Trifluoperazine should be given in reduced dosage to elderly or debilitated patients.

The usual initial *oral* dose for the treatment of schizophrenia and other **psychoses** is 2 to 5 mg twice daily, gradually increased to a usual range of 15 to 20 mg daily; in severe or resistant psychoses daily doses of 40 mg or more have been given. For the control of acute psychotic symptoms it may be given by deep *intramuscular* injection in a dose of 1 to 2 mg, repeated if necessary every 4 to 6 hours; more than 6 mg daily is rarely required. The initial oral dose for use in *children* is up to 5 mg daily in divided doses adjusted according to age, body-weight, and response, or 1 mg given once or twice daily by intramuscular injection.

For the control of **nausea and vomiting** the usual adult *oral* dose is 1 or 2 mg twice daily; up to 6 mg daily may be given in divided doses. *Children* aged 3 to 5 years may be given up to 1 mg daily in divided doses; this may be increased to a maximum of 4 mg daily in children aged 6 to 12 years.

When used as an adjunct in the short-term management of **severe anxiety disorders** doses are similar to those used for the control of nausea and vomiting.

Schizophrenia. A systematic review[1] of the use of trifluoperazine for schizophrenia (p.955) concluded that it appeared to be of similar efficacy to other commonly used classical antipsychotics with a similar profile of adverse effects. However, there did not appear to be good evidence for claims that it was effective for schizophrenia at low doses.

1. Marques LO, *et al.* Trifluoperazine for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 17/05/05).

Preparations
BP 2008: Trifluoperazine Tablets;
USP 31: Trifluoperazine Hydrochloride Injection; Trifluoperazine Hydrochloride Syrup; Trifluoperazine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Stelazine; ***Austral.:*** Stelazine; ***Braz.:*** Stelazine; ***Gr.:*** Stelazine; Stelium; ***India:*** Trinicalm; ***Indon.:*** Stelazine; ***Irl.:*** Stelazine; ***Ital.:*** Modalina; ***Mex.:*** Flupazine; Stelazine; ***NZ:*** Stelazine; ***S.Afr.:*** Stelazine; Terflurazine; ***Spain:*** Eskazine; ***Thai.:*** Psyrazine; Triflumed; Triozine; Triplex; ***Turk.:*** Stilizan; ***UK:*** Stelazine; ***Venez.:*** Leptazine; Taclorpil†.

Multi-ingredient: ***Arg.:*** Cuait D; Cuait N; Stelapar; ***Braz.:*** Stelapar†; ***Canad.:*** Stelabid†; ***India:*** Sycot; Trinicalm Forte; Trinicalm Plus; ***Ital.:*** Parmodalin; ***Mex.:*** Stelabid.

Trifluperidol *(BAN, USAN, rINN)*

McN-JR-2498; R-2498; Triflupéridol; Trifluperidoli; Trifluperidolum. 4′-Fluoro-4-[4-hydroxy-4-(3-trifluoromethylphenyl)piperidino]butyrophenone.

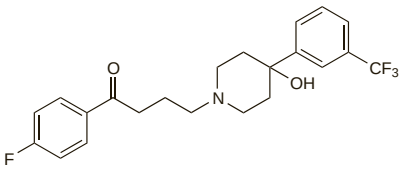
Трифлуперидол

$C_{22}H_{23}F_4NO_2$ = 409.4.

CAS — 749-13-3.

ATC — N05AD02.

ATC Vet — QN05AD02.



Trifluperidol Hydrochloride *(BANM, rINNM)*

Hidrocloruro de trifluperidol; Triflupéridol, Chlorhydrate de; Trifluperidoli Hydrochloridum.

Трифлуперидола Гидрохлорид

$C_{22}H_{23}F_4NO_2$,HCl = 445.9.

CAS — 2062-77-3.

ATC — N05AD02.

ATC Vet — QN05AD02.

Profile

Trifluperidol is a butyrophenone with general properties similar to those of haloperidol (p.1000), and has been used as the hydrochloride in the treatment of psychoses including schizophrenia.

Preparations

Proprietary Preparations (details are given in Part 3)
India: Triperidol.

Triflupromazine *(BAN, rINN)*

Fluopromazine; Triflupromazina; Triflupromazinum. *NN*-Dimethyl-3-(2-trifluoromethylphenothiazin-10-yl)propylamine.

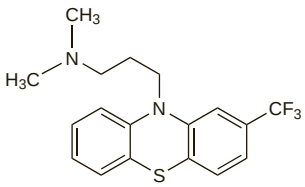
Трифлупромазин

$C_{18}H_{19}F_3N_2S$ = 352.4.

CAS — 146-54-3.

ATC — N05AA05.

ATC Vet — QN05AA05.



Pharmacopoeias. In *US*.

USP 31 (Triflupromazine). A light amber viscous oily liquid that crystallises into large irregular crystals during prolonged storage. Practically insoluble in water. Store in airtight containers. Protect from light.

Triflupromazine Hydrochloride *(BANM, rINNM)*

Fluopromazine Hydrochloride; Hidrocloruro de triflupromazina; Triflupromazine, Chlorhydrate de; Triflupromazini Hydrochloridum.

Трифлупромазина Гидрохлорид

$C_{18}H_{19}F_3N_2S$,HCl = 388.9.

CAS — 1098-60-8.

ATC — N05AA05.

ATC Vet — QN05AA05.

Pharmacopoeias. In *US*.

USP 31 (Triflupromazine Hydrochloride). A white to pale tan crystalline powder having a slight characteristic odour. Soluble 1 in less than 1 of water and of alcohol and 1 in 1.7 of chloroform; soluble in acetone; insoluble in ether. Store in glass containers. Protect from light.

Profile

Triflupromazine hydrochloride is a phenothiazine with general properties similar to those of chlorpromazine (p.969). It is used mainly in the management of psychoses (p.954) and the control of nausea and vomiting (p.1700). Triflupromazine hydrochloride is usually given by injection but in some countries oral preparations are available.

In the management of psychosis, the usual dose is 60 to 150 mg daily by intramuscular injection. For the control of nausea and vomiting 5 to 15 mg is given intramuscularly and repeated after 4 hours if necessary up to a maximum of 60 mg daily; a dose of 1 mg to a maximum total daily dose of 3 mg may be given intravenously.

A suggested intramuscular dose for children over 2 years of age is 200 to 250 micrograms/kg daily up to a maximum of 10 mg daily.

Reduced doses should be used in elderly or debilitated patients.

Preparations

USP 31: Triflupromazine Hydrochloride Injection; Triflupromazine Hydrochloride Tablets; Triflupromazine Oral Solution.

Proprietary Preparations (details are given in Part 3)
Austria: Psyquil; ***Ger.:*** Psyquil†; ***India:*** Siquil.

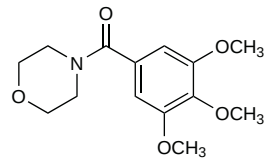
Trimetozine *(USAN, rINN)*

Abbott-22370; NSC-62939; PS-2383; Trimetozina; Trimétozine; Trimetozinum. 4-(3,4,5-Trimethoxybenzoyl)morpholine.

Триметоцин

$C_{14}H_{19}NO_5$ = 281.3.

CAS — 635-41-6.



Profile

Trimetozine has been used for its sedative properties.

Preparations

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

Valnoctamide *(USAN, rINN)*

McN-X-181; NSC-32363; Valnoctamida; Valnoctamidum. 2-Ethyl-3-methylvaleramide.

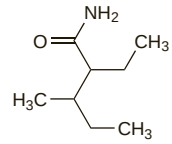
Вальноктамид

$C_8H_{17}NO$ = 143.2.

CAS — 4171-13-5.

ATC — N05CM13.

ATC Vet — QN05CM13.



Profile

Valnoctamide, an isomer of valpromide (p.508), has been given orally in the treatment of anxiety disorders.

◊ References.

1. Bialer M, *et al.* Pharmacokinetics of a valpromide isomer, valnoctamide, in healthy subjects. *Eur J Clin Pharmacol* 1990; **38:** 289–91.
2. Barel S, *et al.* Stereoselective pharmacokinetic analysis of valnoctamide in healthy subjects and in patients with epilepsy. *Clin Pharmacol Ther* 1997; **61:** 442–9.

Interactions. For a discussion of the potential interaction between carbamazepine and valnoctamide, see Antiepileptics, p.474.

Veralipride *(rINN)*

Veraliprida; Véralipride; Veralipridum. *N*-[(1-Allyl-2-pyrrolidinyl)methyl]-5-sulphamoyl-2-veratramide.

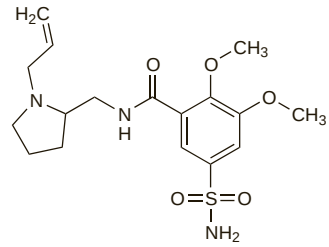
Вералиприд

$C_{17}H_{25}N_3O_5S$ = 383.5.

CAS — 66644-81-3.

ATC — N05AL06.

ATC Vet — QN05AL06.



Profile

Veralipride is a substituted benzamide antipsychotic. It has been used in the treatment of cardiovascular and psychological symptoms associated with the menopause; the usual oral dose is 100 mg daily for 20 days repeated at intervals of 7 to 10 days. Preparations of veralipride have now been withdrawn from the market in some countries because of the opinion that there is an unacceptable balance of risks and benefits; adverse effects such as anxiety, depression, and tardive dyskinesia have been associated with veralipride, both during and after treatment.

Menopausal disorders. HRT with oestrogens is the mainstay of treatment for acute symptoms associated with the menopause (see p.2077) but when it is considered to be unsuitable a variety of other drugs including veralipride have been tried.[1] It has also been tried with raloxifene in postmenopausal women.[2] However, treatment with veralipride has been associated with extrapyramidal adverse effects.[3,4]

1. Young RL, *et al.* Management of menopause when estrogen cannot be used. *Drugs* 1990; **40**: 220–30.
2. Morgante G, *et al.* Veralipride administered in combination with raloxifene decreases hot flushes and improves bone density in early postmenopausal women. *Gynecol Endocrinol* 2004; **18:** 194–8.
3. Masmoudi K, *et al.* Troubles extrapyramidaux sous véralipride (Agréal), traitement symptomatique des bouffées de chaleur: à propos de 17 cas. *Rev Med Interne* 2005; **26:** 453–7.
4. Raja M, Azzoni A. Tardive dyskinesia after long-term veralipride treatment. *J Neuropsychiatr Clin Neurosci* 2005; **17:** 252–3.

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

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Veralipral; ***Belg.:*** Agreal†; ***Braz.:*** Agreal; ***Chile:*** Agreal; ***Fr.:*** Agreal†; ***Ital.:*** Agradil; Veralipril†; ***Mex.:*** Aclimafel; Veraligral; ***Port.:*** Agreal†; ***Spain:*** Agreal†.

Multi-ingredient: ***Arg.:*** Veralipral T.

Zaleplon *(BAN, USAN, rINN)*

CL-284846; L-846; LJC-10846; Tsaleploni; ZAL-846; Zaleplón; Zaléplone; Zaleplonum. 3′-(3-Cyanopyrazolo[1,5-*a*]pyrimidin-7-yl)-*N*-ethylacetanilide.

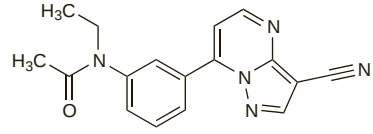
Залеплон

$C_{17}H_{15}N_5O$ = 305.3.

CAS — 151319-34-5.

ATC — N05CF03.

ATC Vet — QN05CF03.



Dependence and Withdrawal

As for Diazepam, p.987.

Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987. Zaleplon should be used with caution and in reduced doses in patients with hepatic impairment, and should be avoided where this is severe.

Treatment of overdose is largely supportive. Activated charcoal may be given orally to patients who present within one hour of ingestion of more than 50 mg zale-