sulfoxide appeared to be compensatorily increased in slow hydroxylators.

1. Axelsson R. On the serum concentrations and antipsychotic effects of thioridazine, thioridazine side-chain sulfoxide and thioridazine side-chain sulfone, in chronic psychotic patients. *Curr Ther Res* 1977; **21:** 587–605.
2. von Bahr C, *et al.* Plasma levels of thioridazine and metabolites are influenced by the debrisoquin hydroxylation phenotype. *Clin Pharmacol Ther* 1991; **49:** 234–40.

Uses and Administration

Thioridazine is a phenothiazine with general properties similar to those of chlorpromazine (p.975). It has a piperidine side-chain and, unlike chlorpromazine, has little antiemetic activity.

The use of thioridazine has been restricted to the treatment of schizophrenia (p.955) in patients who fail to show an adequate response to treatment with other antipsychotics. Its use in other psychiatric disorders was abandoned after it was felt that there was an unacceptable balance of risks and benefits as a result of its cardiotoxic potential; it has been withdrawn in some countries, including the UK.

For all patients starting thioridazine it is recommended that a baseline ECG and electrolyte screening are performed. An ECG should also be repeated before each dose increase, 1 week after the maximum therapeutic dose has been reached, and at 6-monthly intervals in those who continue treatment. Serum electrolyte concentrations should also be monitored periodically during treatment and any imbalance corrected.

Thioridazine is given orally as the hydrochloride or the base, and doses may be expressed in terms of either. In some countries, doses of oral liquid preparations have been given in terms of the base, whereas those of the tablets have been given as the hydrochloride. In the USA, all doses are given in terms of the hydrochloride. Thioridazine 22.8 mg is equivalent to about 25 mg of thioridazine hydrochloride.

In the treatment of schizophrenia thioridazine hydrochloride should be started at the usual dose of 50 to 100 mg three times daily and slowly titrated upwards to a maximum of 800 mg daily if necessary; doses should be reduced once effective control is achieved. The daily dosage range is 200 to 800 mg, which may be given in 2 to 4 divided doses. It has been recommended that increases in doses should be no more than 100 mg weekly.

Thioridazine should be given in lower initial doses to patients with a low body-mass or those with hepatic or renal impairment; dosage increases should also be more gradual.

In those patients who require withdrawal of thioridazine, the dose should be gradually reduced over 1 to 2 weeks to avoid symptoms such as gastrointestinal disorders, dizziness, anxiety, and insomnia that are sometimes seen after abruptly stopping high-dose or long-term treatment.

◊ References.

1. Fenton M, *et al.* Thioridazine for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 25/03/08).

Preparations

USP 31: Thioridazine Hydrochloride Oral Solution; Thioridazine Hydrochloride Tablets; Thioridazine Oral Suspension.

Proprietary Preparations (details are given in Part 3)
Arg.: Melleril†; ***Austral.:*** Aldazine; Melleril†; ***Austria:*** Melleril†; ***Belg.:*** Melleril†; ***Braz.:*** Melleril†; Unitidazin; ***Chile:*** Melleril†; Nervosan†; Simultan; Tinsenol†; ***Denm.:*** Melleril†; ***Fin.:*** Melleril†; Orsanil†; ***Fr.:*** Melleril†; ***Ger.:*** Mellerетten†; Melleril†; ***Gr.:*** Melleril†; ***Hong Kong:*** Melleril†; ***Hung.:*** Melleril†; ***India:*** Thioril; ***Indon.:*** Melleril; ***Irl.:*** Melleril†; Melzine†; Thiozine†; ***Israel:*** Ridazin; ***Ital.:*** Melleril†; ***Malaysia:*** Aldazine†; Melleril†; ***Mex.:*** Dazithin; Melleril†; ***Neth.:*** Melleril†; ***Norw.:*** Melleril†; ***NZ:*** Aldazine; Melleril†; ***Port.:*** Melleril†; ***Rus.:*** Sonapax (Сонапакс); Thiodazine (Тиодазин); Thioril (Тиорил); Tison (Тисон); ***S.Afr.:*** Melleril†; ***Spain:*** Melleril†; ***Swed.:*** Mallorol†; ***Switz.:*** Mellerettes†; Melleril†; ***Thai.:*** Calmaril†; Dazine†; Ridazine; Thiomed; Thiosia; ***Turk.:*** Mellerettes†; Melleril†; ***UK:*** Melleril†; Rideril†; ***USA:*** Mellaril†; ***Venez.:*** Melleril†.

Tiapride Hydrochloride *(BANM, rINNM)*

FLO-1347; Hidrocloruro de tiaprida; Tiapride, chlorhydrate de; Tiaprid-hidroklorid; Tiaprid-hydrochlorid; Tiapridhydroklorid; Tiapridi hydrochloridum; Tiapridihydrokloridi; Tiaprido hidrochloridas. *N*-(2-Diethylaminoethyl)-2-methoxy-5-methylsulphonylbenzamide hydrochloride.

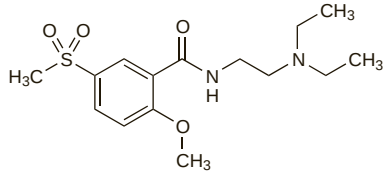
Тиаприда Гидрохлорид

$C_{15}H_{24}N_2O_4S,HCl$ = 364.9.

CAS — 51012-32-9 (tiapride); 51012-33-0 (tiapride hydrochloride).

ATC — N05AL03.

ATC Vet — QN05AL03.



(tiapride)

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

Ph. Eur. 6.2 (Tiapride Hydrochloride). A white or almost white crystalline powder. Very soluble in water; slightly soluble in dehydrated alcohol; soluble in methyl alcohol. A 5% solution in water has a pH of 4.0 to 6.0.

Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969.

Effects on the cardiovascular system. Torsade de pointes developed after a single dose of tiapride in an elderly patient with cardiac disease, a known risk factor for such arrhythmias.[1]

1. Iglesias E, *et al.* Tiapride-induced torsade de pointes. *Am J Med* 2000; **109:** 509.

Interactions

As for Chlorpromazine, p.973.

Pharmacokinetics

Tiapride is rapidly absorbed after oral doses and peak plasma concentrations occur after 1 to 2 hours. It is excreted largely unchanged in the urine. The plasma half-life is reported to range from 3 to 4 hours. It is thought to be distributed into breast milk on the basis of *animal* studies.

◊ The steady-state pharmacokinetics of tiapride have been studied in 5 elderly patients with tardive dyskinesia, and in 2 patients with Huntington's chorea.[1] All patients received tiapride 100 mg three times daily by mouth for 7 days. The mean peak plasma concentration of tiapride was 1.47 micrograms/mL, achieved a mean of 1.4 hours after dosing, and the mean elimination half-life was 3.8 hours. These values did not differ significantly from those previously reported in younger healthy subjects, although renal clearance was slightly lower in these patients. About half of the dose of tiapride was excreted unchanged by the kidneys; a metabolite, probably *N*-monodesethyltiapride was detected in the urine but its identity was not confirmed.

1. Roos RAC, *et al.* Pharmacokinetics of tiapride in patients with tardive dyskinesia and Huntington's disease. *Eur J Clin Pharmacol* 1986; **31:** 191–4.

Uses and Administration

Tiapride is a substituted benzamide with general properties similar to those of sulpiride (p.1028).

It is usually given as the hydrochloride in the management of behavioural disorders and to treat dyskinesias. Doses are expressed in terms of the equivalent amount of base; tiapride hydrochloride 222.2 mg is equivalent to about 200 mg of tiapride. Oral doses of 200 to 400 mg daily are usually given, although higher daily doses have been used, particularly in the management of dyskinesias. Tiapride hydrochloride has also been given by intramuscular or intravenous injection.

Disturbed behaviour. For a discussion of the management of disturbed behaviour including limitations on the use of antipsychotics, see p.954.

References.

1. Gutzmann H, *et al.* Measuring the efficacy of psychopharmacological treatment of psychomotoric restlessness in dementia: clinical evaluation of tiapride. *Pharmacopsychiatry* 1997; **30:** 6–11.
2. Allain H, *et al.* Double blind study of tiapride versus haloperidol and placebo in agitation and aggressiveness in elderly patients with cognitive impairment. *Psychopharmacology (Berl)* 2000; **148:** 361–6.

Extrapyramidal disorders. Tiapride has been tried in the treatment of antipsychotic-induced tardive dyskinesia (p.971), but, as with all antipsychotics, improvement may only be short-term.

Tiapride has also been tried in the treatment of Tourette's syndrome (p.954).

For reference to the use of tiapride in suppressing the adverse effects of levodopa on respiration, see p.806.

CHOREA. Antipsychotics have some action against choreiform movements as well as being of use to control the behavioural disturbances of Huntington's chorea, and tiapride has been quite widely used for this purpose. For a discussion of the management of various choreas, see p.953.

References.

1. Roos RAC, *et al.* Tiapride in the treatment of Huntington's chorea. *Acta Neurol Scand* 1982; **65:** 45–50.
2. Deroover J, *et al.* Tiapride versus placebo: a double-blind comparative study in the management of Huntington's chorea. *Curr Med Res Opin* 1984; **9:** 329–38.

Substance dependence. An early review[1] concluded that the role of tiapride in acute *alcohol* withdrawal (p.1626) was likely to be limited as patients at risk of severe reactions would still require adjunctive therapy for the control of hallucinations and seizures. Following detoxification, tiapride appeared to help, to some degree, to alleviate distress, improve abstinence and drinking behaviour, and facilitate reintegration within society.[2] Interest in its use with carbamazepine continues.[3-5]

1. Peters DH, Faulds D. Tiapride: a review of its pharmacology and therapeutic potential in the management of alcohol dependence syndrome. *Drugs* 1994; **47:** 1010–32.
2. Shaw GK, *et al.* Tiapride in the prevention of relapse in recently detoxified alcoholics. *Br J Psychiatry* 1994; **165:** 515–23.
3. Franz M, *et al.* Treatment of alcohol withdrawal: tiapride and carbamazepine versus clomethiazole: a pilot study. *Eur Arch Psychiatry Clin Neurosci* 2001; **251:** 185–92.
4. Lucht M, *et al.* Alcohol withdrawal treatment in intoxicated vs non-intoxicated patients: a controlled open-label study with tiapride/carbamazepine, clomethiazole and diazepam. *Alcohol Alcohol* 2003; **38:** 168–75.
5. Soyka M, *et al.* Efficacy and safety of outpatient alcohol detoxification with a combination of tiapride/carbamazepine: additional evidence. *Pharmacopsychiatry* 2006; **39:** 30–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Etiles†; ***Austria:*** Delpral; ***Belg.:*** Tiapridal; ***Braz.:*** Tiapridal; ***Chile:*** Sereprid; ***Cz.:*** Tiapra; Tiapridal; ***Fr.:*** Clemental†; Equilium†; Tiapridal; ***Ger.:*** Tiapridex; ***Gr.:*** Tiapridal; ***Hong Kong:*** Tiapridal†; ***Hung.:*** Tiapridal; ***Israel:*** Doparid; ***Ital.:*** Italprid; Sereprile; ***Jpn:*** Gramalil; ***Neth.:*** Betaprid; Elbaprid; Tiacob; Tiajac; Tiapridal; Tiastad; Tiazet; ***Pol.:*** Tiapridal; ***Port.:*** Normagit†; Tiapridal; ***Rus.:*** Tiapridal (Тиапридал); ***Spain:*** Tiaprizal; ***Switz.:*** Tiapridal.

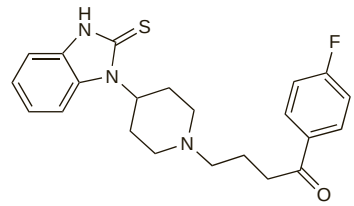
Timiperone *(rINN)*

DD-3480; Timiperona; Timipérone; Timiperonum. 4′-Fluoro-4-[4-(2-thioxo-1-benzimidazolinyl)piperidino]butyrophenone.

Тимиперон

$C_{22}H_{24}FN_3OS$ = 397.5.

CAS — 57648-21-2.



Profile

Timiperone is a butyrophenone with general properties similar to those of haloperidol (p.1000). It has been used by mouth in the treatment of schizophrenia. Timiperone has also been given by injection.

Tiotixene *(BAN, rINN)*

NSC-108165; P-4657B; Thiothixene *(USAN)*; Tiotikseeni; Tiotixen; Tiotixène; Tiotixeno; Tiotixenum. (*Z*)-*NN*-Dimethyl-9-[3-(4-methylpiperazin-1-yl)propylidene]thioxanthene-2-sulphonamide.

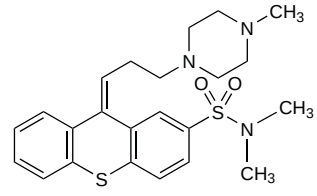
Тиотиксен

$C_{23}H_{29}N_3O_2S_2$ = 443.6.

CAS — 5591-45-7; 3313-26-6 (tiotixene Z-isomer).

ATC — N05AF04.

ATC Vet — QN05AF04.



cis-form

Pharmacopoeias. In *US.*

USP 31 (Thiothixene). White to tan, practically odourless, crystals. Practically insoluble in water; soluble 1 in 110 of dehydrated alcohol, 1 in 2 of chloroform, and 1 in 120 of ether; slightly soluble in acetone and in methyl alcohol. Store in airtight containers. Protect from light.

Tiotixene Hydrochloride *(BANM, rINNM)*

CP-12252-1; Hidrocloruro de tiotixeno; Thiothixene Hydrochloride *(USAN)*; Tiotixène, Chlorhydrate de; Tiotixeni Hydrochloridum.

Тиотиксена Гидрохлорид

$C_{23}H_{29}N_3O_2S_2,2HCl,2H_2O$ = 552.6.

CAS — 58513-59-0 (anhydrous tiotixene hydrochloride); 49746-04-5 (anhydrous tiotixene hydrochloride, Z-isomer); 22189-31-7 (tiotixene hydrochloride dihydrate); 49746-09-0 (tiotixene hydrochloride dihydrate, Z-isomer).

ATC — N05AF04.

ATC Vet — QN05AF04.

Pharmacopoeias. In *US*, which permits both the dihydrate and the anhydrous form.

USP 31 (Thiothixene Hydrochloride). It is anhydrous ($C_{23}H_{29}N_3O_2S_2,2HCl$ = 516.5) or contains two molecules of water of hydration. A white or practically white crystalline powder

having a slight odour. Soluble 1 in 8 of water, 1 in 270 of dehydrated alcohol, and 1 in 280 of chloroform; practically insoluble in acetone, in ether, and in benzene. Store in airtight containers. Protect from light.

Stability. A combination of the stabilisers hydroxyquinoline sulfate and vanillin could protect tiotixene from photodegradation.[1]

1. Thoma K, Klimek R. Photostabilization of drugs in dosage forms without protection from packaging materials. *Int J Pharmaceutics* 1991; **67:** 169–75.

Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969. Tiotixene is less likely to cause sedation but extrapyramidal effects are more frequent.

Interactions

As for Chlorpromazine, p.973.

Pharmacokinetics

◊ In 15 adequately controlled schizophrenic patients receiving oral tiotixene 15 to 60 mg daily in 2, 3, or 4 divided doses, plasma concentrations were found to be in the relatively narrow range of 10 to 22.5 nanograms/mL 126 to 150 minutes after the last daily dose despite the fourfold difference in dosage.[1] Investigations in a further 5 patients indicated that peak plasma concentrations were obtained about 1 to 3 hours after a dose, indicating rapid absorption with an absorption half-time of about 30 minutes. There was an early plasma half-life of about 210 minutes and a late half-life of about 34 hours; resurgence of drug concentrations in some subjects might have been due to enterohepatic recycling.

1. Hobbs DC, *et al*. Pharmacokinetics of thiothixene in man. *Clin Pharmacol Ther* 1974; **16:** 473–8.

Metabolism. There has been a study[1] indicating that tiotixene may induce its own metabolism.

1. Bergling R, *et al*. Plasma levels and clinical effects of thioridazine and thiothixene. *J Clin Pharmacol* 1975; **15:** 178–86.

Uses and Administration

Tiotixene is a thioxanthene antipsychotic with general properties similar to those of the phenothiazine, chlorpromazine (p.975). It has a piperazine side-chain. It is used in the treatment of psychoses including schizophrenia (p.955). Tiotixene is given orally as the base or hydrochloride and by intramuscular injection as the hydrochloride. Doses are expressed in terms of the base. Tiotixene 1 mg is equivalent to about 1.2 mg of tiotixene hydrochloride.

The usual initial oral dose is 2 mg three times daily (or 5 mg twice daily in more severe conditions) gradually increasing to 20 to 30 mg daily if necessary; once-daily dosage may be adequate. In severe or resistant psychoses doses of up to 60 mg daily may be given. The usual initial intramuscular dose is 4 mg two to four times daily increased if necessary to a maximum of 30 mg daily.

Tiotixene should be given in reduced dosage to elderly or debilitated patients.

Preparations

USP 31: Thiothixene Capsules; Thiothixene Hydrochloride for Injection; Thiothixene Hydrochloride Injection; Thiothixene Hydrochloride Oral Solution.

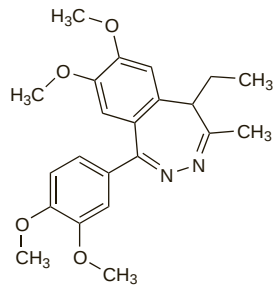
Proprietary Preparations (details are given in Part 3)
Austral.: Navane; ***Canad.:*** Navane; ***Hong Kong:*** Navane; ***Neth.:*** Navane†; ***NZ:*** Thixit; ***USA:*** Navane.

Tofisopam *(rINN)*

EGYT-341; Tofisopaami; Tofisopamum; Tofizopam. 1-(3,4-Dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5*H*-2,3-benzodiazepine.

Тофизопам

$C_{22}H_{26}N_2O_4$ = 382.5.
CAS — 22345-47-7.
ATC — N05BA23.
ATC Vet — QN05BA23.



Pharmacopoeias. In *Jpn.*

Profile

Tofisopam is a 2,3-benzodiazepine related structurally to the 1,4-benzodiazepines such as diazepam (p.986) and sharing some of the same actions. It is reported, however, to be largely lacking in the sedative, anticonvulsant, and muscle relaxant properties of the conventional benzodiazepines. Tofisopam has been given orally in the short-term treatment of anxiety disorders. The *R*-(+)-isomer, dextofisopam, is under investigation in the treatment of irritable bowel syndrome.

Preparations

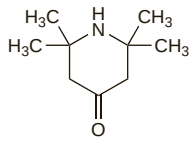
Proprietary Preparations (details are given in Part 3)
Cz.: Grandaxin; ***Hung.:*** Grandaxin; ***Jpn:*** Grandaxin; ***Rus.:*** Grandaxin (Грандаксин); ***Thai.:*** Grandaxin.

Triacetonamine Tosilate

Tempidon. 2,2,6,6-Tetramethyl-4-piperidone-toluenesulfonate.

Триацетонамина Тозилат

$C_{16}H_{25}NO_4S$ = 327.4.
CAS — 826-36-8 (triacetonamine); 29334-13-2 (triacetonamine tosilate).



(triacetonamine)

Profile

Triacetonamine tosilate has anxiolytic actions and is used in combination preparations with analgesics.

Preparations

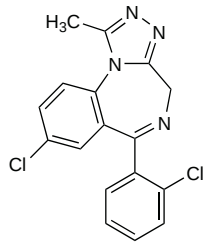
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Rus.:*** Tempalgin (Темпалгин); Tempanginol (Темпангинол).

Triazolam *(BAN, USAN, rINN)*

Clorazolam; Triatsolaami; Triazolamum; U-33030. 8-Chloro-6-(2-chlorophenyl)-1-methyl-4*H*-[1,2,4]triazolo[4,3-*a*][1,4]benzodiazepine.

Триазолам

$C_{17}H_{12}Cl_2N_4$ = 343.2.
CAS — 28911-01-5.
ATC — N05CD05.
ATC Vet — QN05CD05.



Pharmacopoeias. In *Chin.* and *US.*

USP 31 (Triazolam). A white to off-white, practically odourless, crystalline powder. Practically insoluble in water and in ether; soluble 1 in 1000 of alcohol, 1 in 25 of chloroform, and 1 in 600 of 0.1N hydrochloric acid.

Dependence and Withdrawal

As for Diazepam, p.987.

Adverse Effects and Treatment

As for Diazepam, p.987.

Effects on the liver. A 44-year-old man developed severe pruritus with jaundice which subsequently proved fatal. Liver histology showed intense cholestasis. Triazolam was considered to be the most likely cause.[1]

1. Cobden I, *et al*. Fatal intrahepatic cholestasis associated with triazolam. *Postgrad Med J* 1981; **57:** 730–1.

Effects on mental function. The effects of triazolam on mental function have been controversial since van der Kroef first described in 1979 a range of symptoms including anxiety, amnesia, depersonalisation and derealisation, depression, paranoia, and severe suicidal tendencies that he had seen in 25 patients and attributed to triazolam.[1] This led to suspension of triazolam in the Netherlands (re-approved in 1990) and removal of the 1-mg tablet from other markets. Continued reporting of similar symptoms of cognitive impairment with triazolam resulted in withdrawal of the 500-microgram dosage form in several countries in 1987 and 1988 and in a gradual reduction of recommended dosage from 1 mg at night down to 125 to 250 micrograms at night. Triazolam was withdrawn from the UK[2] and some other markets in 1991. Opinion still remains divided over the adverse effects of triazolam, the main issues being its propensity to cause adverse effects relative to other benzodiazepines and whether its risk-benefit ratio is acceptable to justify its continued use.[3,4]

Others[5] have reviewed spontaneous adverse effects reported to the FDA in the USA for triazolam, temazepam, and flurazepam. Daytime sedation was noted with all three, but triazolam caused more agitation, confusion, hallucinations, and amnesia. Such effects occurred frequently with the 250-microgram dose as well as with the 500-microgram dose. Similar results were obtained after analysis of reports for triazolam and temazepam in the first 7 years of marketing, although the possibility that selection factors were producing higher reporting rates for triazolam could not be entirely excluded.[6] A study[7] gave triazolam 500 micrograms, lormetazepam 2 mg, or placebo, to groups of 40 patients for 25 nights and observed the greatest frequency of daytime anxiety, panic, derealisation, and paranoia with triazolam. Another[8] found a greater total number of reports of memory impairment or amnesia after nightly doses of triazolam 500 micrograms compared with temazepam 30 mg. Triazolam also impaired delayed, but not immediate, memory recall. Similar cases of memory impairment occurring with triazolam at doses of 125 and 250 micrograms have reportedly been submitted to the UK CSM.[2] The emergence of daytime symptoms after more than a few days' treatment with triazolam could be attributed to rebound or withdrawal phenomena occurring as a result of rapid elimination of the drug.

As regards the risk-benefit ratio of triazolam some workers have questioned the hypnotic efficacy of the drug at a dose of 250 micrograms and consider that reduction of the dose has decreased efficacy more than adverse effects.[3]

In defence of triazolam, the FDA and the manufacturers (*Upjohn*) have considered epidemiological studies which, unlike the FDA spontaneous reporting scheme, have been unable to demonstrate a substantial difference in its adverse effects compared with other benzodiazepines except, perhaps, in the incidence of amnesia.[9] Retrospective studies[10,11] claiming similar findings have been the subject of criticism.[12-14] Other workers have cited studies indicating benefit of triazolam 250 micrograms for the treatment of insomnia.[15] A review by the US Institute of Medicine found that triazolam was safe when given in a dose of 250 micrograms daily for 7 to 10 days but called for studies of lower doses and of long-term use.[16]

1. Van der Kroef C. Reactions to triazolam. *Lancet* 1979; **ii:** 526.
2. Anonymous. The sudden withdrawal of triazolam—reasons and consequences. *Drug Ther Bull* 1991; **29:** 89–90.
3. O'Donovan MC, McGuffin P. Short acting benzodiazepines. *BMJ* 1993; **306:** 945–6.
4. Ghaeli P, *et al.* Triazolam treatment controversy. *Ann Pharmacother* 1994; **28:** 1038–40.
5. Bixler EO, *et al.* Adverse reactions to benzodiazepine hypnotics: spontaneous reporting system. *Pharmacology* 1987; **35:** 286–300.
6. Wysowski DK, Barash D. Adverse behavioral reactions attributed to triazolam in the Food and Drug Administration's spontaneous reporting system. *Arch Intern Med* 1991; **151:** 2003–8.
7. Adam K, Oswald I. Can a rapidly-eliminated hypnotic cause daytime anxiety? *Pharmacopsychiatry* 1989; **22:** 115–19.
8. Bixler EO, *et al.* Next-day memory impairment with triazolam use. *Lancet* 1991; **337:** 827–31.
9. Drucker RF, MacLeod N. Benzodiazepines. *Pharm J* 1989; **243:** 508.
10. Hindmarch I, *et al.* Adverse events after triazolam substitution. *Lancet* 1993; **341:** 55.
11. Rothschild AJ, *et al.* Triazolam and disinhibition. *Lancet* 1993; **341:** 186.
12. Hawley CJ, *et al.* Adverse events after triazolam substitution. *Lancet* 1993; **341:** 567.
13. Vela-Bueno A. Adverse events after triazolam substitution. *Lancet* 1993; **341:** 567.
14. Kales A, *et al.* Adverse events after triazolam substitution. *Lancet* 1993; **341:** 567–8.
15. Gillin JC, Byerley WF. Diagnosis and management of insomnia. *N Engl J Med* 1990; **323:** 487.
16. Ault A. FDA advisers find no major Halcion dangers. *Lancet* 1997; **350:** 1760.

Precautions

As for Diazepam, p.988.

Hepatic impairment. Cirrhosis decreased the apparent oral clearance of triazolam to an extent depending on the severity of the liver disease.[1] An initial dose of 125 micrograms was suggested for patients with severe liver dysfunction. It was suggested that the relative lack of effect that mild to moderate cirrhosis had on the metabolism of oral triazolam might be due to some first-pass metabolism occurring in the intestinal wall.[2]

1. Kroboth PD, *et al*. Nighttime dosing of triazolam in patients with liver disease and normal subjects: kinetics and daytime effects. *J Clin Pharmacol* 1987; **27:** 555–60.
2. Robin DW, *et al.* Triazolam in cirrhosis: pharmacokinetics and pharmacodynamics. *Clin Pharmacol Ther* 1993; **54:** 630–7.

Renal impairment. Peak plasma-triazolam concentrations were lower in 11 dialysis patients compared with 11 controls.[1] It was postulated that a relatively high basal gastric acid secretion in dialysis patients could result in hydrolysis and opening of the ring structure of triazolam effectively reducing its systemic avail-