The ECG effects of fexofenadine have been studied[3] in normal subjects and doses of up to 480 mg daily [4 times the recommended dose for seasonal allergic rhinitis] did not prolong the QT interval. See also p.562.

1. Pinto YM, *et al.* QT lengthening and life-threatening arrhythmias as associated with fexofenadine. *Lancet* 1999; **353:** 980.
2. Giraud T. QT lengthening and arrhythmias associated with fexofenadine. *Lancet* 1999; **353:** 2072.
3. Pratt CM, *et al.* Cardiovascular safety of fexofenadine HCl. *Am J Cardiol* 1999; **83:** 1451–4.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving fexofenadine, and the American Academy of Pediatrics[1] considers that it is therefore usually compatible with breast feeding.

See also under Adverse Effects and Precautions, in Terfenadine, p.590.

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 08/04/04)

Psoriasis. Exacerbation of psoriasis has been reported[1] in association with the use of fexofenadine.

1. Saraswat A, Saraswat M. Pustular exacerbation of psoriasis due to fexofenadine. *Clin Exp Dermatol* 2006; **31:** 477–8.

Interactions

As for the non-sedating antihistamines in general, p.563.

Plasma concentrations of fexofenadine have been increased when given with erythromycin or ketoconazole, but, unlike terfenadine, licensed product information states that this was not associated with adverse effects on the QT interval.

Antacids containing aluminium and magnesium hydroxide have reduced the absorption of fexofenadine. Fruit juices including grapefruit may reduce the bioavailability of fexofenadine and use together should be avoided.

◊ References.

1. Dresser GK, *et al.* Effect of grapefruit juice volume on the reduction of fexofenadine bioavailability: possible role of organic anion transporting polypeptides. *Clin Pharmacol Ther* 2005; **77:** 170–7.

Pharmacokinetics

Fexofenadine is rapidly absorbed after oral doses with peak plasma concentrations being reached in 2 to 3 hours. It is about 60 to 70% bound to plasma proteins. About 5% of the total dose is metabolised, mostly by the intestinal mucosa, with only 0.5 to 1.5% of the dose undergoing hepatic biotransformation by the cytochrome P450 system. Elimination half-life of about 14 hours has been reported although this may be prolonged in patients with renal impairment. Excretion is mainly in the faeces with only 10% being present in the urine. Fexofenadine does not appear to cross the blood-brain barrier.

Fexofenadine is a metabolite of terfenadine and as such has been detected in breast milk after the administration of terfenadine.

◊ References.

1. Russell T, *et al.* Pharmacokinetics, pharmacodynamics, and tolerance of single- and multiple-dose fexofenadine hydrochloride in healthy male volunteers. *Clin Pharmacol Ther* 1998; **64:** 612–21.

Uses and Administration

Fexofenadine, an active metabolite of terfenadine (p.590), is a non-sedating antihistamine. It does not possess significant sedative or antimuscarinic actions. Fexofenadine is used as the hydrochloride in the symptomatic relief of allergic conditions including seasonal allergic rhinitis (p.565) and chronic urticaria (p.565).

In the UK a dose of fexofenadine hydrochloride 120 mg once daily is given orally in the treatment of seasonal allergic rhinitis; the recommended dose in chronic idiopathic urticaria is 180 mg once daily. US licensed product information suggests a dose of 60 mg twice daily or 180 mg once daily for both indications.

Fexofenadine is also used with a decongestant such as pseudoephedrine hydrochloride.

For doses in children or in patients with renal impairment, see below.

◊ References.

1. Markham A, Wagstaff AJ. Fexofenadine. *Drugs* 1998; **55:** 269–74.
2. Simpson K, Jarvis B. Fexofenadine: a review of its use in the management of seasonal allergic rhinitis and chronic idiopathic urticaria. *Drugs* 2000; **59:** 301–21.
3. Kawashima M, *et al.* Review of fexofenadine in the treatment of chronic idiopathic urticaria. *Int J Dermatol* 2002; **41:** 701–6.
4. Meeves SG, Appajosyula S. [Aventis, USA]. Efficacy and safety profile of fexofenadine HCl: a unique therapeutic option in H1-receptor antagonist treatment. *J Allergy Clin Immunol* 2003; **112** (suppl): S69–S77.
5. Mansfield LE. Once-daily immediate-release fexofenadine and sustained-release pseudoephedrine combination: a new treatment option for allergic rhinitis. *Expert Opin Pharmacother* 2006; **7:** 941–51.

Administration in children. Fexofenadine hydrochloride is used in children for the treatment of seasonal allergic rhinitis in an oral dose of 30 mg twice daily; in the UK it is licensed for use in children aged 6 to 11 years whereas in the USA it may be used in children as young as 2 years.

In the USA, fexofenadine is also licensed for use in paediatric chronic idiopathic urticaria. The dose in children aged 6 months to less than 2 years is 15 mg twice daily; older children may be given 30 mg twice daily.

For suggested doses in children with renal impairment see below.

Administration in renal impairment. US licensed product information recommends that initial oral doses of fexofenadine hydrochloride in adults with renal impairment should be reduced to 60 mg once daily. In children with renal impairment, the initial dose should be reduced to 30 mg once daily in patients aged 2 to 11 years, and to 15 mg once daily in children aged 6 months to less than 2 years.

UK product information advises that fexofenadine should be given with caution to patients with renal impairment; however, it also states that dose adjustment is not considered to be necessary in such patients.

Preparations

USP 31: Fexofenadine Hydrochloride and Pseudoephedrine Hydrochloride Extended-Release Tablets; Fexofenadine Hydrochloride Capsules; Fexofenadine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Alerfedine; Allegra; Fexofen†; ***Austral.:*** Fexotabs; Telfast; Xergic; ***Austria:*** Telfast; ***Belg.:*** Telfast; ***Braz.:*** Allegra; Altiva; ***Canad.:*** Allegra; ***Chile:*** Aerodan; Alexia; Allegra; Fenax; ***Cz.:*** Afexil; Ewofex; Telfast; ***Denm.:*** Telfast; ***Fin.:*** Telfast; ***Fr.:*** Telfast; ***Ger.:*** Telfast; ***Hong Kong:*** Telfast; ***Hung.:*** Altiva; Telfast; ***India:*** Alermex†; Allegra; Fexigra; Fexofen; Fexova; Odifex; ***Indon.:*** Telfast; ***Irl.:*** Telfast; ***Israel:*** Telfast; ***Ital.:*** Kalicet†; Telfast; ***Malaysia:*** Telfast; ***Mex.:*** Allegra; ***Neth.:*** Telfast; ***Norw.:*** Telfast; ***NZ:*** Telfast; Xergic; ***Philipp.:*** Telfast; ***Pol.:*** Telfast; ***Port.:*** Telfast; ***Rus.:*** Fexadin (Фексадин); Telfast (Телфаст); ***S.Afr.:*** Telfast; ***Singapore:*** Telfast; ***Spain:*** Telfast; ***Swed.:*** Telfast; ***Switz.:*** Telfast; ***Thai.:*** Fenafex; Telfast; ***Turk.:*** Fexadyne; Fexofen; Telfast; ***UK:*** Telfast; ***USA:*** Allegra; ***Venez.:*** Allegra; Fexidine; Fexoril; Rinolast.

Multi-ingredient: ***Arg.:*** Alerfedine D; Allegra-D; ***Austral.:*** Telfast Decongestant; ***Braz.:*** Allegra-D; ***Canad.:*** Allegra-D; ***Chile:*** Alexia D; Allegra-D; ***Hong Kong:*** Telfast-D; ***Indon.:*** Telfast Plus; ***Malaysia:*** Altiva-D; Telfast-D; ***Mex.:*** Allegra-D; ***NZ:*** Telfast Decongestant†; ***Singapore:*** Telfast-D; ***USA:*** Allegra-D; ***Venez.:*** Allegra-D; Rinolast D.

Flunarizine Hydrochloride *(BANM, USAN, rINNM)*

Flunaritsiinidihydrokloridi; Flunarizin-dihydrochlorid; Flunarizindihydroklorid; Flunarizine, Chlorhydrate de; Flunarizine, dichlorhydrate de; Flunarizini dihydrochloridum; Flunarizini Hydrochloridum; Flunarizino dihidrochloridas; Hidrocloruro de flunarizina; R-14950. *trans*-1-Cinnamyl-4-(4,4′-difluorobenzhydryl)piperazine dihydrochloride.

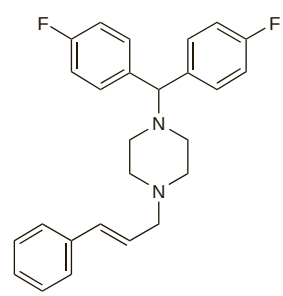
Флунаризина Гидрохлорид

$C_{26}H_{26}F_2N_2.2HCl = 477.4$.

CAS — 52468-60-7 (flunarizine); 30484-77-6 (flunarizine hydrochloride).

ATC — N07CA03.

ATC Vet — QN07CA03.



(flunarizine)

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

Ph. Eur. 6.2 (Flunarizine Dihydrochloride). A white or almost white hygroscopic powder. Slightly soluble in water, in alcohol, and in dichloromethane; sparingly soluble in methyl alcohol. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for the sedating antihistamines in general, p.561. Adverse effects also seen with flunarizine include weight gain, extrapyramidal symptoms (sometimes associated with depression), and, rarely, galactorrhoea.

Extrapyramidal disorders. Extrapyramidal motor signs (including parkinsonism, orofacial tardive dyskinesia, and akathisia) have been reported in 12 patients given flunarizine 10 to 40 mg daily for between 3 weeks and 15 months; 11 also had mental depression.[1] Partial or complete improvement of symptoms occurred after withdrawal of flunarizine. There have been other reports of similar effects,[2-5] but the association with flunarizine has not always been certain. Some workers have commented that flunarizine is often used in patients at increased risk of depression (migraine and geriatric patients) or extrapyramidal symptoms (geriatric patients)[2,6] or that flunarizine may unmask subclinical idiopathic Parkinson's disease.[6,7]

Extrapyramidal signs, including parkinsonism, have also been associated with the related drug, cinnarizine.[3-5] It has been suggested that such effects may be less likely to occur with cinnarizine than with flunarizine because of its shorter half-life and lower lipophilicity.[3]

1. Chouza C, *et al.* Parkinsonism, tardive dyskinesia, akathisia, and depression induced by flunarizine. *Lancet* 1986; **i:** 1303–4.
2. Meyboom RHB, *et al.* Parkinsonism, tardive dyskinesia, akathisia, and depression induced by flunarizine. *Lancet* 1986; **ii:** 292.
3. Laporte J-R, Capella D. Useless drugs are not placebos: lessons from flunarizine and cinnarizine. *Lancet* 1986; **ii:** 853–4.
4. Laporte J-R, Capella D. Useless drugs are not placebos. *Lancet* 1987; **i:** 1324.
5. Teive HAG, *et al.* Flunarizine and cinnarizine-induced parkinsonism: a historical and clinical analysis. *Parkinsonism Relat Disord* 2004; **10:** 243–5.
6. Amery W. Side-effects of flunarizine. *Lancet* 1986; **i:** 1497.
7. Benvenuti F, *et al.* Side-effects of flunarizine. *Lancet* 1986; **ii:** 464.

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

Interactions

As for the sedating antihistamines in general, p.563.

Hepatic enzyme inducers such as carbamazepine, phenytoin, and valproate may interact with flunarizine by increasing its metabolism; an increase in dosage of flunarizine may be required.

Pharmacokinetics

Flunarizine hydrochloride is well absorbed from the gastrointestinal tract, peak plasma concentrations occurring 2 to 4 hours after oral doses. Flunarizine hydrochloride is very lipophilic and is more than 90% bound to plasma proteins. It appears to undergo extensive metabolism; metabolites are excreted principally in the bile. Flunarizine hydrochloride has an elimination half-life of about 18 days.

Uses and Administration

Flunarizine is the difluorinated derivative of cinnarizine. It has antihistamine, sedative, and calcium-channel blocking activity. Flunarizine hydrochloride is used for migraine prophylaxis, for vertigo and vestibular disorders, and for peripheral and cerebral vascular disorders. It has also been used as adjunctive antiepileptic therapy in patients refractory to standard regimens.

Flunarizine is given orally as the hydrochloride although doses are expressed in terms of the base. Flunarizine hydrochloride 11.8 mg is equivalent to about 10 mg of flunarizine. The usual dose is 5 to 10 mg daily, usually given at night to minimise the effects of drowsiness.

Epilepsy. A number of drugs with calcium-channel blocking activity have been investigated as adjuncts in epilepsy (p.465), including flunarizine. Some individual studies have reported benefit, but a systematic review[1] concluded that although flunarizine might have a weak effect on seizure frequency the evidence was not convincing, and the withdrawal rate was significant, probably because of poor tolerability; it should therefore not be recommended as adjunctive antiepileptic therapy. The pharmacokinetic profile of flunarizine may in any case be too complex for clinical use as an antiepileptic.[2]

1. Chaisewikul R, *et al.* Calcium antagonists as an add-on therapy for drug-resistant epilepsy. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2001 (accessed 13/06/05).
2. Hoppu K, *et al.* Flunarizine of limited value in children with intractable epilepsy. *Pediatr Neurol* 1995; **13:** 143–7.

Migraine. Flunarizine reduces the frequency of migraine attacks in both adult and paediatric patients and is used for the prophylaxis of migraine (p.616) in some countries. Its effects are comparable with several other prophylactic antimigraine drugs, including the generally preferred propranolol,[1-4] but it is more likely to be reserved for use when first-line drugs have proved to be ineffective or unsuitable. Its mode of action in migraine is unclear; possible mechanisms are inhibition of vasospasm induced by mediators such as serotonin and prostaglandins, inhibition of

cellular hypoxia, and improved blood viscosity and erythrocyte deformability. Calcium-channel blocking activity might have a role, but evidence for the efficacy of other calcium-channel blockers in migraine prophylaxis (see Nifedipine, p.1355) is less convincing than for flunarizine.

Case reports have indicated benefit with flunarizine in the prophylaxis of the rare disorder of alternating hemiplegia in childhood[5,6] but a subsequent study[7] in 12 children did not produce conclusive findings. A later long-term study[8] reported that 7 of 9 children given flunarizine for up to 5 years for hemiplegia showed a reduction in the duration of attacks, and 3 had a reduction in frequency, but only 1 of these obtained a complete cessation of episodes.

The role of antihistamines in general in the management of migraine is discussed briefly on p.564.

1. Todd PA, Benfield P. Flunarizine: a reappraisal of its pharmacological properties and therapeutic use in neurological disorders. *Drugs* 1989; **38:** 481–99.
2. Andersson K-E, Vinge E. β-Adrenoceptor blockers and calcium antagonists in the prophylaxis and treatment of migraine. *Drugs* 1990; **3:** 355–73.
3. Soelberg Sørensen P, *et al.* Flunarizine versus metoprolol in migraine prophylaxis: a double-blind, randomized parallel group study of efficacy and tolerability. *Headache* 1991; **31:** 650–7.
4. Gawel MJ, *et al.* Comparison of the efficacy and safety of flunarizine to propranolol in the prophylaxis of migraine. *Can J Neurol Sci* 1992; **19:** 340–5.
5. Casaer P, Azou M. Flunarizine in alternating hemiplegia in childhood. *Lancet* 1984; **ii:** 579.
6. Curatolo P, Cusmai R. Drugs for alternating hemiplegic migraine. *Lancet* 1984; **ii:** 980.
7. Casaer P. Flunarizine in alternating hemiplegia in childhood. An international study in 12 children. *Neuropediatrics* 1987; **18:** 191–5.
8. Silver K, Andermann F. Alternating hemiplegia of childhood: a study of 10 patients and results of flunarizine treatment. *Neurology* 1993; **43:** 36–41.

Tourette's syndrome. A small unblinded study[1] involving 7 patients has suggested that flunarizine is more effective than placebo in the treatment of Tourette's syndrome (see Tics, p.954).

1. Micheli F, *et al.* Treatment of Tourette's syndrome with calcium antagonists. *Clin Neuropharmacol* 1990; **13:** 77–83.

Vertigo. Antihistamines are the mainstay of the treatment of vertigo (p.565). However, their antimuscarinic adverse effects may prove troublesome, particularly in the elderly, and they produce central sedation. Flunarizine is devoid of antimuscarinic properties, although it may produce central sedation.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Bercetina; Coromert; Flufenal; Mondus; Niflucan; Sibelium; Vasculoflex†; ***Austria:*** Amalium; Flunarium; Sibelium; ***Belg.:*** Flunarimed; Flunatop; Kelamigra; Sibelium; ***Braz.:*** Flunarin; Fluvert; Fluzix; Sibelium; Vertigium; Vertix; ***Canad.:*** Sibelium; ***Chile:*** Flerox; Fluxus; Irrigor; Sibelium; Zentralin; ***Cz.:*** Sibelium; ***Denm.:*** Sibelium; ***Fr.:*** Sibelium; ***Ger.:*** Flunavert; Natil-N; Sibelium; ***Gr.:*** Sibelium; ***Hong Kong:*** Fludan; Sibelium†; ***Hung.:*** Sibelium; ***India:*** Migarid; Nomigrain; ***Indon.:*** Bartolium; Cevadil; Degnium; Dizilium; Frego; Sibelium; Sibenid; Silum; Sinral; Unalium; Xepalium; ***Irl.:*** Sibelium; ***Ital.:*** Flugeral; Flunagen; Fluxarten; Gradient; Issium; Sibelium; Vasculene; ***Malaysia:*** Fludan; Forknow; Migarid; Sibelium; ***Mex.:*** Axilin; Fasolan; Naflurył; Sibelium; ***Neth.:*** Sibelium; ***Philipp.:*** Sibelium; ***Port.:*** Sibelium; Vasilium; Zinasen; ***S.Afr.:*** Sibelium; ***Singapore:*** Forknow; Narizine†; Sibelium†; ***Spain:*** Flerudin; Flurpax; Sibelium; ***Switz.:*** Sibelium; ***Thai.:*** Cedelate†; Finelium†; Floxin; Fludan; Flulium; Flunarium; Flunaza†; Flunazine†; Fluricin; Hexilium; Liberal; Medilium; Poli-Flunarin; Seabell†; Sibelium; Simoyiam; Sobelin; Vanid; Vertilium; Zelium; ***Turk.:*** Sibelium; ***Venez.:*** Fludil; Sibelium.

Multi-ingredient: *Arg.:* Angiolit†; CCK Flunarizina†; Sibelium Plus; ***Braz.:*** Vertizine D.

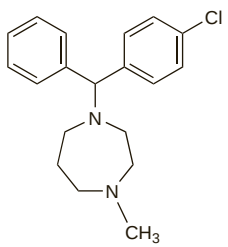
Homochlorcyclizine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de homoclorciclizina; Homochlorcyclizine, Chlorhydrate d'; Homochlorcyclizini Hydrochloridum. 1-(4-Chlorobenzhydryl)perhydro-4-methyl-1,4-diazepine dihydrochloride.

Гомохлорциклизина Гидрохлорид

$C_{19}H_{23}ClN_2,2HCl$ = 387.8.

CAS — 848-53-3 (homochlorcyclizine); 1982-36-1 (homochlorcyclizine hydrochloride).



(homochlorcyclizine)

Pharmacopoeias. In *Jpn.*

Profile

Homochlorcyclizine hydrochloride, a piperazine derivative, is a sedating antihistamine (p.561) with antimuscarinic and moderate sedative properties. It is used for the symptomatic relief of allergic conditions including urticaria (p.565) and rhinitis (p.565), and in pruritic skin disorders (p.565). It is given in oral doses of 10 to 20 mg three times daily.

Preparations

Proprietary Preparations (details are given in Part 3)

Hong Kong: Homoclomin; ***Indon.:*** Homoclomin; ***Jpn:*** Homoclomin; ***Thai.:*** Homoclomin.

Hydroxyzine *(BAN, rINN)*

Hidroxizina; Hydroksitsiini; Hydroxizin; Hydroxyzinum. (*RS*)-2-{2-[4-(*p*-Chloro-α-phenylbenzyl)piperazin-1-yl]ethoxy}ethanol.

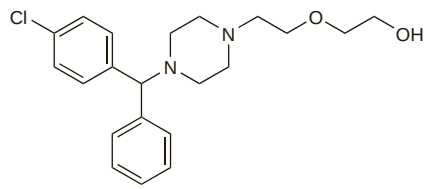
Гидроксизин

$C_{21}H_{27}ClN_2O_2$ = 374.9.

CAS — 68-88-2.

ATC — N05BB01.

ATC Vet — QN05BB01.



Hydroxyzine Embonate *(BANM, rINNM)*

Embonato de hidroxizina; Hydroxyzine, Embonate d'; Hydroxyzine Pamoate; Hydroxyzini Embonas; Pamoato de hidroxizina. 2-{2-[4-(4-Chlorobenzhydryl)piperazin-1-yl]ethoxy}ethanol 4,4′-methylenebis(3-hydroxy-2-naphthoate).

Гидроксизина Эмбонат

$C_{21}H_{27}ClN_2O_2,C_{23}H_{16}O_6$ = 763.3.

CAS — 10246-75-0.

ATC — N05BB01.

ATC Vet — QN05BB01.

Pharmacopoeias. In *Jpn* and *US.*

USP 31 (Hydroxyzine Pamoate). A light yellow, practically odourless powder. Soluble 1 in more than 1000 of water, of chloroform, and of ether, 1 in 700 of alcohol, 1 in 10 of dimethylformamide, and 1 in 3.5 of 10M sodium hydroxide solution; practically insoluble in methyl alcohol. Store in airtight containers.

Hydroxyzine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de hidroxizina; Hidroksizin Hidroklorür; Hidroksizino hidrochloridas; Hydroxizin-hidroklorid; Hydroksitsiinihydrokloridi; Hydroxizinhydrokloríd; Hydroxyzin dihydrochlorid; Hydroxyzine, chlorhydrate d'; Hydroxyzini Dihydrochloridum; Hydroxyzini hydrochloridum.

Гидроксизина Гидрохлорид

$C_{21}H_{27}ClN_2O_2,2HCl$ = 447.8.

CAS — 2192-20-3.

ATC — N05BB01.

ATC Vet — QN05BB01.

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

Ph. Eur. 6.2 (Hydroxyzine Hydrochloride). A white or almost white, crystalline, hygroscopic powder. Freely soluble in water and in alcohol; very slightly soluble in acetone. Store in airtight containers. Protect from light.

USP 31 (Hydroxyzine Hydrochloride). A white, odourless, powder. Soluble 1 in 1 of water, 1 in 4.5 of alcohol, and 1 in 13 of chloroform; slightly soluble in acetone; practically insoluble in ether. Store in airtight containers.

Incompatibility. Hydroxyzine hydrochloride has been reported to be incompatible with aminophylline, benzylpenicillin salts, chloramphenicol sodium succinate, dimenhydrinate, doxorubicin hydrochloride (in a liposomal formulation), thioridazine, and some soluble barbiturates.

Stability. A mixture of hydroxyzine hydrochloride, chlorpromazine hydrochloride, and pethidine hydrochloride stored in glass or plastic syringes was found[1] to be stable for 366 days at 4° and 25°.

1. Conklin CA, *et al.* Stability of an analgesic-sedative combination in glass and plastic single-dose syringes. *Am J Hosp Pharm* 1985; **42:** 339–42.

Adverse Effects and Precautions

As for the sedating antihistamines in general, p.561.

Intramuscular injection of hydroxyzine has been reported to cause marked local discomfort. Intravenous use has been associated with haemolysis.

Amputation. Accidental intra-arterial injection of hydroxyzine has led to necrosis of the extremity requiring amputation of the digits of the affected limb.[1]

1. Hardesty WH. Inadvertent intra-arterial injection. *JAMA* 1970; **213:** 872.

Arrhythmias. ECG abnormalities, particularly alterations in T-waves, were associated with anxiolytic doses of hydroxyzine hydrochloride and were similar to those produced by thioridazine and tricyclic antidepressants.[1]

1. Hollister LE. Hydroxyzine hydrochloride: possible adverse cardiac interactions. *Psychopharmacol Comm* 1975; **1:** 61–5.

Effects on sexual function. A 32-year-old man had prolonged penile erections (priapism) after taking two separate doses of hydroxyzine for a skin rash.[1] It was suggested that the effect might be due to a hydroxyzine metabolite that was found to be structurally similar to a metabolite of trazodone, a drug known to induce penile erections.

1. Thavundayil JX. *et al.* Prolonged penile erections induced by hydroxyzine: possible mechanism of action. *Neuropsychobiology* 1994; **30:** 4–6.

Effects on the skin. Four children given hydroxyzine hydrochloride for restlessness developed a fixed drug eruption of the penis.[1] All recovered on drug withdrawal and subsequently had positive rechallenges.

1. Cohen HA, *et al.* Fixed drug eruption of the penis due to hydroxyzine hydrochloride. *Ann Pharmacother* 1997; **31:** 327–9.

Liver disorders. A study[1] has suggested that hydroxyzine should only be given once daily for the relief of pruritus in patients with primary biliary cirrhosis. The mean serum elimination half-lives of hydroxyzine and its metabolite cetirizine in 8 patients with primary biliary cirrhosis were 36.6 and 25.0 hours respectively.

1. Simons FER, *et al.* The pharmacokinetics and pharmacodynamics of hydroxyzine in patients with primary biliary cirrhosis. *J Clin Pharmacol* 1989; **29:** 809–15.

Porphyria. Hydroxyzine has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

As for the sedating antihistamines in general, p.563.

Pharmacokinetics

Hydroxyzine is rapidly absorbed from the gastrointestinal tract and is metabolised. Metabolites include cetirizine (p.570), which has antihistaminic activity. An elimination half-life of about 20 hours has been reported.

◊ References.

1. Paton DM, Webster DR. Clinical pharmacokinetics of H -receptor antagonists (the antihistamines). *Clin Pharmacokinet* 1985; **10:** 477–97.

Liver disorders. For reference to a prolonged half-life of hydroxyzine in patients with primary biliary cirrhosis, see under Adverse Effects and Precautions, above.

Uses and Administration

Hydroxyzine, a piperazine derivative, is a sedating antihistamine with antimuscarinic and significant sedative properties; it is also an antiemetic. Its main use is as an anxiolytic (p.952) but see Anxiety Disorders below. It is also used as an adjunct to pre- and postoperative medication (see Anaesthesia, p.563) and in the management of pruritus (p.565) and urticaria (p.565) and has been used as an adjunct to opioid analgesia in the management of cancer pain (p.5).

Hydroxyzine may be given orally as the hydrochloride or the embonate; doses are expressed in terms of the hydrochloride. Hydroxyzine embonate 170 mg is equivalent to about 100 mg of hydroxyzine hydrochloride.

The usual oral doses in adults are: 50 to 100 mg four times daily for the short-term management of anxiety; for pruritus an initial dose of 25 mg given at night, increased if necessary to 25 mg three or four times daily; and 50 to 100 mg for pre- or postoperative sedation. For pruritus in children over 6 years of age the initial dose is 15 to 25 mg daily increased if necessary to 50 to 100 mg daily in divided doses; for children 6 months to 6 years old the initial dose is 5 to 15 mg daily increased if necessary to 50 mg daily in divided doses.