tion; Fluphenazine Hydrochloride Oral Solution; Fluphenazine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Austral.: Anatensol†; Modecate; ***Austria:*** Dapotum; ***Belg.:*** Sevinol†; ***Braz.:*** Flufenan; ***Canad.:*** Modecate; Moditen†; ***Chile:*** Modecate; ***Cz.:*** Moditen; ***Denm.:*** Pacinol†; Siqualone; ***Fin.:*** Pacinol†; Siqualone; ***Fr.:*** Modecate; Moditen; ***Ger.:*** Dapotum; Lyogen; Lyorodin; Omca; ***Hong Kong:*** Modecate; ***Hung.:*** Moditen; ***India:*** Anatensol; Fludecan; ***Indon.:*** Anatensol; Modecate; ***Irl.:*** Modecate; ***Israel:*** Fludecate; ***Ital.:*** Anatensol; Moditen; ***Malaysia:*** Deca; ***Mex.:*** Siqualine; ***Neth.:*** Anatensol; Moditen; ***Norw.:*** Siqualone; ***NZ:*** Anatensol; Modecate; ***Philipp.:*** Modezine; Shrizine; Sydepres; ***Port.:*** Anatensol; Cenilene†; Phenazin; ***Rus.:*** Moditen (Модитен); ***S.Afr.:*** Fludecate; Modecate; ***Singapore:*** Modecate; ***Spain:*** Modecate; ***Swed.:*** Pacinol†; Siqualone; ***Switz.:*** Dapotum; ***Thai.:*** Deca; Fluzine†; Pharnazine; Phenazine†; Potensone†; ***Turk.:*** Prolixin; ***UK:*** Modecate; Moditen†; ***USA:*** Prolixin†; ***Venez.:*** Moditen.

Multi-ingredient: ***Braz.:*** Diserim; ***Chile:*** Motitrel; ***Indon.:*** Motival; ***Irl.:*** Motival; ***Ital.:*** Dominans; ***Mex.:*** Motival; ***S.Afr.:*** Motival; ***Thai.:*** Cetavol; ***UK:*** Motival†.

Flurazepam *(BAN, rINN)*

Fluratsepaami; Flurazépam; Flurazepamum. 7-Chloro-1-(2-diethylaminoethyl)-5-(2-fluorophenyl)-1,3-dihydro-1,4-benzodiazepin-2-one.

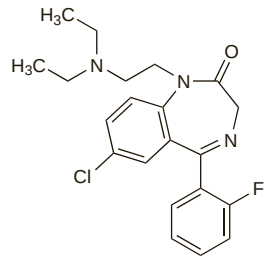
Флуразепам

$C_{21}H_{23}ClFN_3O$ = 387.9.

CAS — 17617-23-1.

ATC — N05CD01.

ATC Vet — QN05CD01.



Pharmacopoeias. In *Jpn.*

Flurazepam Monohydrochloride *(BANM, rINNM)*

Fluratsepaamimonohydrokloridi; Flurazepam hydrochlorid; Flurazépam, monochlorhydrate de; Flurazepami Hydrochloridum; Flurazepami monohydrochloridum; Flurazepám-monohidroklorid; Flurazepammonohydroklorid; Flurazepamo monohidrochloridas; Monochidrocloruro de flurazepam.

Флуразепама Моногидрохлорид

$C_{21}H_{23}ClFN_3O$,HCl = 424.3.

CAS — 36105-20-1.

ATC — N05CD01.

ATC Vet — QN05CD01.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn.*
Ph. Eur. 6.2 (Flurazepam Monohydrochloride). A white or almost white crystalline powder. Very soluble in water; freely soluble in alcohol. A 5% solution in water has a pH of 5.0 to 6.0. Protect from light.

Flurazepam Dihydrochloride *(BANM, rINNM)*

Dihidrocloruro de flurazepam; Flurazépam, Dichlorhydrate de; Flurazepam Hydrochloride *(USAN)*; Flurazepami Dihydrochloridum; NSC-78559; Ro-5-6901.

Флуразепама Дигидрохлорид

$C_{21}H_{23}ClFN_3O$,2HCl = 460.8.

CAS — 1172-18-5.

ATC — N05CD01.

ATC Vet — QN05CD01.

Pharmacopoeias. In *Chin.* and *US.*
USP 31 (Flurazepam Hydrochloride). An off-white to yellow crystalline powder. Is odourless or has a slight odour. Soluble 1 in 2 of water, 1 in 4 of alcohol, 1 in 90 of chloroform, 1 in 3 of methyl alcohol, 1 in 69 of isopropyl alcohol, 1 in 5000 of ether and of petroleum spirit, and 1 in 2500 of benzene. A solution in water is acid to litmus. Store in airtight containers. Protect from light.

Dependence and Withdrawal

As for Diazepam, p.987.

Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987.

Effects on the liver. Reports of cholestatic jaundice after the use of flurazepam.[1,2]

1. Fang MH, *et al*. Cholestatic jaundice associated with flurazepam hydrochloride. *Ann Intern Med* 1978; **89:** 363–4.
2. Reynolds R, *et al.* Cholestatic jaundice induced by flurazepam hydrochloride. *Can Med Assoc J* 1981; **124:** 893–4.

Effects on taste. Flurazepam had been reported to cause dysgeusia.[1]

1. Willoughby JMT. Drug-induced abnormalities of taste sensation. *Adverse Drug React Bull* 1983 (June): 368–71.

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

Renal impairment. Five patients on maintenance haemodialysis developed encephalopathy attributed to flurazepam and diazepam.[1]

1. Taclob L, Needle M. Drug-induced encephalopathy in patients on maintenance haemodialysis. *Lancet* 1976; **ii:** 704–5.

Interactions

As for Diazepam, p.989.

Pharmacokinetics

Flurazepam is readily absorbed from the gastrointestinal tract. It undergoes extensive first-pass metabolism and is excreted in the urine, chiefly as conjugated metabolites. The major active metabolite is *N*-desalkylflurazepam, which is reported to have a half-life ranging from 47 to 100 hours or more.

Metabolism. The metabolism of flurazepam was studied in 4 healthy male subjects given 30 mg daily for 2 weeks.[1] A hydroxyethyl metabolite was present in the blood shortly after a dose. The *N*-desalkyl metabolite, the major metabolite in the blood, had a half-life ranging from 47 to 100 hours. Steady-state concentrations were reached after 7 to 10 days and were about 5 to 6 times greater than those observed on day 1. Results from a study in 3 patients indicated that some metabolism of flurazepam may occur in the small bowel mucosa.[2]

1. Kaplan SA, *et al*. Blood level profile in man following chronic oral administration of flurazepam hydrochloride. *J Pharm Sci* 1973; **62:** 1932–5.
2. Mahon WA, *et al.* Metabolism of flurazepam by the small intestine. *Clin Pharmacol Ther* 1977; **22:** 228–33.

Uses and Administration

Flurazepam is a long-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 the USA flurazepam is given as the dihydrochloride and doses are expressed in terms of this salt. Flurazepam dihydrochloride 30 mg is equivalent to about 25.3 mg of flurazepam. Doses of 15 to 30 mg orally at night are given. In the UK flurazepam is given as the monohydrochloride although doses are expressed in terms of the base; flurazepam monohydrochloride 32.8 mg is equivalent to about 30 mg of flurazepam. Doses equivalent to 15 to 30 mg of flurazepam at night are given. A maximum initial dose of 15 mg has been suggested in the UK and the USA for elderly or debilitated patients.

Preparations

BP 2008: Flurazepam Capsules;
USP 31: Flurazepam Hydrochloride Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Fordrim†; ***Austria:*** Staurodorm; ***Belg.:*** Staurodorm; ***Braz.:*** Dalmadorm; ***Canad.:*** Dalmane†; ***Ger.:*** Dalmadorm; Staurodorm Neu; ***Hong Kong:*** Dalmadorm; ***India:*** Fluraz; ***Indon.:*** Dalmadorm; ***Irl.:*** Dalmane; ***Ital.:*** Dalmadorm; Felison; Flunox; Remdue; Valdorm; ***Neth.:*** Dalmadorm; ***Port.:*** Dalmadorm; Morfex; ***S.Afr.:*** Dalmadorm; ***Singapore:*** Dalmadorm; ***Spain:*** Dormodor; ***Switz.:*** Dalmadorm; ***Thai.:*** Dalmadorm; ***UK:*** Dalmane; ***USA:*** Dalmane†; ***Venez.:*** Fluralema.

Fluspirilene *(BAN, USAN, rINN)*

Fluspirileeni; Fluspirilen; Fluspirilenas; Fluspirilène; Fluspirileno; Fluspirilenum; McN-JR-6218; R-6218. 8-[4,4-Bis(4-fluorophenyl)butyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one.

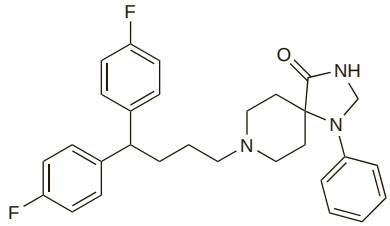
Флуспирилен

$C_{29}H_{31}F_2N_3O$ = 475.6.

CAS — 1841-19-6.

ATC — N05AG01.

ATC Vet — QN05AG01.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Fluspirilene). A white or almost white powder. It exhibits polymorphism. Practically insoluble in water; slightly soluble in alcohol; soluble in dichloromethane. Protect from light.

Profile

Fluspirilene is a diphenylbutylpiperidine antipsychotic and has general properties similar to those of the phenothiazine, chlorpromazine (p.969). It is less likely to cause sedation. Fluspirilene has been given by deep intramuscular injection for the treatment of psychoses including schizophrenia (p.955). A usual initial dose is up to 2 mg weekly by deep intramuscular injection, increased according to response. Usual maintenance doses have ranged from 1 to 10 mg weekly although higher doses have been used in exceptional cases.

Adverse effects. References.

1. McCreadie RG, *et al*. Probable toxic necrosis after prolonged fluspirilene administration. *BMJ* 1979; **1:** 523–4.

Schizophrenia. A systematic review[1] found that evidence to support the use of depot fluspirilene over oral chlorpromazine or other depot antipsychotics in the treatment of schizophrenia was lacking.

1. Abhijnhan A, *et al.* Depot fluspirilene for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 18/03/08).

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Imap; ***Belg.:*** Imap; ***Cz.:*** Imap†; ***Ger.:*** Fluspi; Imap; kivat†; ***Irl.:*** Redeptin†; ***Neth.:*** Imap.

Gepirone Hydrochloride *(USAN, rINNM)*

BMY-13805-1; Gépirone, Chlorhydrate de; Gepironi Hydrochloridum; Hidrocloruro de gepirona; MJ-13805-1; Org-33062 (gepirone). 3,3-Dimethyl-*N*-{4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl}glutarimide hydrochloride.

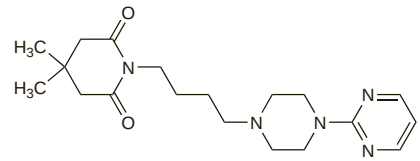
Гепирона Гидрохлорид

$C_{19}H_{29}N_5O_2$,HCl = 395.9.

CAS — 83928-76-1 (gepirone); 83928-66-9 (gepirone hydrochloride).

ATC — N06AX19.

ATC Vet — QN06AX19.



(gepirone)

Profile

Gepirone is structurally related to buspirone (p.965). It has been investigated as the hydrochloride for the treatment of depression and anxiety disorders.

Action. Gepirone is a partial agonist at serotonin (hydroxytryptamine, 5-HT) receptors of the 5-HT_{1A} subtype. For reference to the actions and potential uses of such drugs, see Buspirone, p.966.

References.

1. Feiger AD. A double-blind comparison of gepirone extended release, imipramine, and placebo in the treatment of outpatient major depression. *Psychopharmacol Bull* 1996; **32:** 659–65.
2. Rickels K, *et al*. Gepirone and diazepam in generalized anxiety disorder: a placebo-controlled trial. *J Clin Psychopharmacol* 1997; **17:** 272–7.
3. Dogterom PP, *et al.* Pharmacokinetics of gepirone (Org 33062) in subjects with normal renal function and in patients with chronic renal dysfunction. *Clin Pharmacol Ther* 2002; **71:** P95.
4. Feiger AD, *et al.* Gepirone extended-release: new evidence for efficacy in the treatment of major depressive disorder. *J Clin Psychiatry* 2003; **64:** 243–9.
5. Robinson DS, *et al.* A review of the efficacy and tolerability of immediate-release and extended-release formulations of gepirone. *Clin Ther* 2003; **25:** 1618–33.