Fluphenazine *(BAN, rINN)*

Flufenatsiini; Flufenazin; Flufenazina; Fluphénazine; Fluphenazinum. 2-{4-[3-(2-Trifluoromethylphenothiazin-10-yl)propyl]piperazin-1-yl}ethanol.

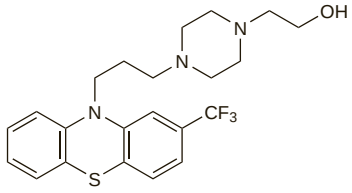
Флуфеназин

$C_{22}H_{26}F_3N_3OS$ = 437.5.

CAS — 69-23-8.

ATC — N05AB02.

ATC Vet — QN05AB02.



Fluphenazine Decanoate *(BANM, rINNM)*

Decanoato de flufenazina; Flufenatsiinidekanoaatti; Flufenazin Dekanoat; Flufenazindekanoat; Flufenazin-dekanoát; Flufenazine-dekanoát; Flufenazino dekanoatas; Fluphénazine, décanoate de; Fluphenazini decanoas.

Флуфеназина Деканоат

$C_{32}H_{44}F_3N_3O_2S$ = 591.8.

CAS — 5002-47-1.

ATC — N05AB02.

ATC Vet — QN05AB02.

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

Ph. Eur. 6.2 (Fluphenazine Decanoate). A pale yellow viscous liquid or a yellow solid. Practically insoluble in water; very soluble in dehydrated alcohol and in dichloromethane; freely soluble in methyl alcohol. Protect from light.

USP 31 (Fluphenazine Decanoate). Store in airtight containers. Protect from light.

Fluphenazine Enantate *(BANM, rINNM)*

Enantato de flufenazina; Flufenatsiinienantaatti; Flufenazinenantat; Flufenazin-enantát; Flufenazino enantatas; Fluphénazine, enantate de; Fluphenazine Enanthate; Fluphenazine Heptanoate; Fluphenazini enantas.

Флуфеназина Энантат

$C_{29}H_{38}F_3N_3O_2S$ = 549.7.

CAS — 2746-81-8.

ATC — N05AB02.

ATC Vet — QN05AB02.

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

Ph. Eur. 6.2 (Fluphenazine Enantate). A pale yellow viscous liquid or a yellow solid. Practically insoluble in water; very soluble in dehydrated alcohol and in dichloromethane; freely soluble in methyl alcohol. Protect from light.

USP 31 (Fluphenazine Enanthate). A pale yellow to yellow-orange, clear to slightly turbid, viscous liquid having a characteristic odour. Insoluble in water; soluble 1 in less than 1 of alcohol and of chloroform and 1 in 2 of ether. Stable in air at room temperature but unstable in strong light. Store in airtight containers. Protect from light.

Fluphenazine Hydrochloride *(BANM, rINNM)*

Flufenatsiinihydrokloridi; Flufenazin-dihydrochlorid; Flufenazin-hidroklorid; Flufenazinhydroklorid; Flufenazino hidrochloridas; Flufenazyny chlorowodorek; Fluphénazine, chlorhydrate de; Fluphenazine Dihydrochloride; Fluphenazini Dihydrochloridum; Fluphenazini hydrochloridum; Hidrocloruro de flufenazina.

Флуфеназина Гидрохлорид

$C_{22}H_{26}F_3N_3OS,2HCl$ = 510.4.

CAS — 146-56-5.

ATC — N05AB02.

ATC Vet — QN05AB02.

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

Ph. Eur. 6.2 (Fluphenazine Dihydrochloride). A white or almost white, crystalline powder. Freely soluble in water; slightly soluble in alcohol and in dichloromethane. A 5% solution in water has a pH of 1.9 to 2.4. Protect from light.

USP 31 (Fluphenazine Hydrochloride). A white or nearly white, odourless crystalline powder. Soluble 1 in 1.4 of water and 1 in 6.7 of alcohol; slightly soluble in acetone and in chloroform; practically insoluble in ether and in benzene. Store in airtight containers. Protect from light.

Adverse Effects and Treatment

As for Chlorpromazine, p.969. Fluphenazine is less likely to cause sedation, hypotension, or antimuscarinic effects but is associated with a higher incidence of extrapyramidal effects.

Convulsions. For mention of fluphenazine as one of the antipsychotics suitable for patients at risk of seizures, see p.969.

Effects on the liver. A patient developed jaundice 17 days after the first of 3 injections of a depot antipsychotic containing fluphenazine decanoate given over a 2-week period.[1] The patient developed indicators of severe liver toxicity, with extreme hyperbilirubinaemia and raised liver enzyme values, and remained very ill for the next 4 months. The patient showed cross-sensitivity to haloperidol but not to flupentixol.

See also under Chlorpromazine, p.971.

1. Kennedy P. Liver cross-sensitivity to antipsychotic drugs. *Br J Psychiatry* 1983; **143:** 312.

Overdosage. A patient who took about 30 fluphenazine hydrochloride 2.5-mg tablets was treated with gastric lavage.[1] Twenty hours after hospital admission he had difficulty in breathing due to spasm of the respiratory muscles; other very severe extrapyramidal adverse effects were also present. Muscle spasm was controlled by diazepam.

There were few adverse effects in a patient given intramuscular fluphenazine decanoate 50 mg every 4 hours, instead of the intended 4 weeks, to a total of 1050 mg.[2] About 3 weeks after the period of overdosage the patient had some degree of hypothermia and tachycardia, and after a further week parkinsonian signs appeared. No specific treatment was given.

1. Ladhani FM. Severe extrapyramidal manifestations following fluphenazine overdose. *Med J Aust* 1974; **2:** 26.
2. Cheung HK, Yu ECS. Effect of 1050 mg fluphenazine decanoate given intramuscularly over six days. *BMJ* 1983; **286:** 1016–17.

Precautions

As for Chlorpromazine, p.972. Fluphenazine may exacerbate depression and therefore it is contra-indicated in severely depressed patients.

Pregnancy. A neonate delivered to a mother who had received fluphenazine hydrochloride 10 to 20 mg daily throughout pregnancy had nasal congestion with severe rhinorrhoea, respiratory distress, vomiting, and extrapyramidal symptoms. Respiratory symptoms appeared to respond to pseudoephedrine.

1. Nath SP, *et al.* Severe rhinorrhea and respiratory distress in a neonate exposed to fluphenazine hydrochloride prenatally. *Ann Pharmacother* 1996; **30:** 35–7.

Interactions

As for Chlorpromazine, p.973.

Pharmacokinetics

Fluphenazine hydrochloride is absorbed after oral doses, and has a reported plasma half-life of 14.7 hours after oral doses. Fluphenazine decanoate and fluphenazine enantate are very slowly absorbed from the site of subcutaneous or intramuscular injection. They both gradually release fluphenazine into the body and are therefore suitable for use as depot injections. The plasma half-life of fluphenazine decanoate has been reported to be 6 to 9 days after intramuscular injection.

◊ References[1-4] to the pharmacokinetics of fluphenazine.

The plasma half-life of fluphenazine after a single dose was 14.7 hours in 1 patient given the hydrochloride orally and 14.9 and 15.3 hours in 2 patients given the hydrochloride by intramuscular injection.[1] The half-life was 3.6 and 3.7 days in 2 patients given the enantate intramuscularly and 9.6 and 6.8 days in 2 patients given the decanoate intramuscularly. Peak plasma-fluphenazine concentrations occurred earlier in patients given fluphenazine decanoate compared with those who received the enantate. Fluphenazine sulfoxide and 7-hydroxyfluphenazine were identified in the urine and faeces.

1. Curry SH, *et al.* Kinetics of fluphenazine after fluphenazine dihydrochloride, enanthate and decanoate administration to man. *Br J Clin Pharmacol* 1979; **7:** 325–31.
2. Wistedt B, *et al.* Slow decline of plasma drug and prolactin levels after discontinuation of chronic treatment with depot neuroleptics. *Lancet* 1981; **i:** 1163.
3. Midha KK, *et al.* Kinetics of oral fluphenazine disposition in humans by GC-MS. *Eur J Clin Pharmacol* 1983; **25:** 709–11.
4. Marder SR, *et al.* Plasma levels of parent drug and metabolites in patients receiving oral and depot fluphenazine. *Psychopharmacol Bull* 1989; **25:** 479–82.

Uses and Administration

Fluphenazine is a phenothiazine with general properties similar to those of chlorpromazine (p.975). It has a piperazine side-chain. Fluphenazine is used in the treatment of psychiatric disorders including schizophrenia (p.955), mania (see Bipolar Disorder, p.372), severe anxiety (p.952), and behavioural disturbances (p.954). Fluphenazine is given as the hydrochloride by mouth or sometimes by intramuscular injection; for both routes, doses are expressed in terms of fluphenazine hydrochloride. The longer-acting decanoate or enantate esters of fluphenazine are given by intramuscular or sometimes subcutaneous injection; for both esters, doses are expressed in terms of the ester.

The usual initial *oral* dose of the hydrochloride for the treatment of schizophrenia, mania, and other **psychoses** is 2.5 to 10 mg daily in two or three divided doses; the dose is then increased according to response up to a usual maximum of 20 mg daily, although higher doses have occasionally been given. Dosage may subsequently be reduced to a usual maintenance dose of 1 to 5 mg daily. A lower initial dose of 1 to 2.5 mg daily, increased according to response up to a maximum of 10 mg daily, is recommended in the elderly. Treatment is sometimes started with an initial *intramuscular* injection of 1.25 mg of the hydrochloride adjusted thereafter according to response. The usual initial intramuscular daily dose is 2.5 to 10 mg given in divided doses every 6 to 8 hours. In general the required parenteral doses of fluphenazine hydrochloride have been found to be about one-third to one-half of those given orally. When symptoms are controlled, oral maintenance therapy may be substituted.

The long-acting decanoate or enantate esters of fluphenazine are usually given by deep intramuscular injection and are used mainly for the *maintenance* treatment of patients with schizophrenia or other chronic psychoses. The onset of action is usually within 1 to 3 days of injection and significant effects on psychosis are usually evident within 2 to 4 days. An initial dose of fluphenazine decanoate 12.5 mg (6.25 mg in the elderly) is given intramuscularly. Subsequent adjustments in the amounts and the dosage interval should be made according to the patient's response; the amounts required may range from 12.5 to 100 mg and the intervals required may range from 2 weeks to 5 or 6 weeks. Lower doses may be possible in some patients (see Schizophrenia, below). If doses greater than 50 mg are considered necessary, cautious increments should be made in steps of 12.5 mg. The enantate ester of fluphenazine has been given in a similar dose range at intervals of 1 to 3 weeks.

Fluphenazine hydrochloride has also been given *orally* in initial doses of 1 mg twice daily, increased if necessary to 2 mg twice daily, for the short-term adjunctive management of severe **anxiety** or **behavioural disturbances**.

Schizophrenia. References[1-3] to fluphenazine decanoate in schizophrenia (p.955) indicating that low doses (10 mg or less every 2 weeks) may be effective in some patients. Use of standard doses at greater intervals (6 weeks) has also been tried.[4] A systematic review of the use of depot fluphenazine in schizophrenia found little advantage over oral use in terms of compliance.[5] Another systematic review[6] considered that although oral fluphenazine is inexpensive and widely available, other drugs may be preferable because of its adverse effects.

1. Kane JM, *et al.* Low-dose neuroleptic treatment of outpatient schizophrenics: I preliminary results for relapse rates. *Arch Gen Psychiatry* 1983; **40:** 893–6.
2. Marder SR, *et al.* Low- and conventional-dose maintenance therapy with fluphenazine decanoate: two-year outcome. *Arch Gen Psychiatry* 1987; **44:** 581–21.
3. Hogarty GE, *et al.* Dose of fluphenazine, familial expressed emotion, and outcome in schizophrenia: results of a two-year controlled study. *Arch Gen Psychiatry* 1988; **45:** 797–805.
4. Carpenter WT, *et al.* Comparative effectiveness of fluphenazine decanoate injections every 2 weeks versus every 6 weeks. *Am J Psychiatry* 1999; **156:** 412–18.
5. David A, *et al.* Depot fluphenazine decanoate and enanthate for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2004 (accessed 14/04/05).
6. Matar HE, AlMerie MQ. Oral fluphenazine versus placebo for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 18/03/08).

Tourette's syndrome. Fluphenazine has been tried[1] as an alternative to standard dopamine antagonists such as haloperidol or pimozide in the symptomatic management of Tourette's syndrome (p.954).

1. Singer HS, *et al.* Haloperidol, fluphenazine and clonidine in tourette syndrome: controversies in treatment. *Pediatr Neurosci* 1985–86; **12:** 71–4.

Preparations

BP 2008: Fluphenazine Decanoate Injection; Fluphenazine Tablets;
USP 31: Fluphenazine Decanoate Injection; Fluphenazine Enanthate Injection; Fluphenazine Hydrochloride Elixir; Fluphenazine Hydrochloride Injec-

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.

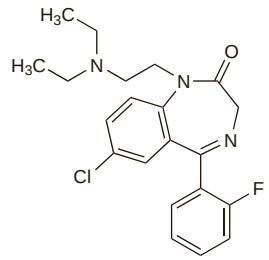
Флуразепам

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

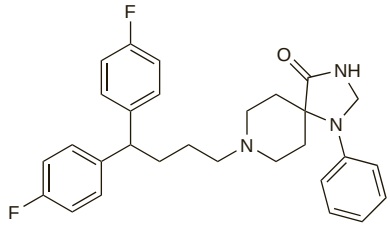
Флуспирилен

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

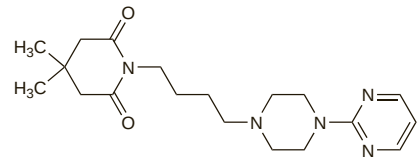
Гепирона Гидрохлорид

$C_{19}H_{29}N_5O_2$,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.