results in 10 of 14 patients with hypochondriasis (p.954) who completed 12 weeks of treatment.[2] Fluvoxamine[3] and paroxetine[4] have also been tried.

1. Fallon BA, *et al.* The pharmacotherapy of hypochondriasis. *Psychopharmacol Bull* 1996; **32:** 607–11.
2. Fallon BA, *et al.* Fluoxetine for hypochondriacal patients without major depression. *J Clin Psychopharmacol* 1993; **13:** 438–41.
3. Fallon BA, *et al.* An open trial of fluvoxamine for hypochondriasis. *Psychosomatics* 2003; **44:** 298–303.
4. Oosterbaan DB, *et al.* An open study of paroxetine in hypochondriasis. *Prog Neuropsychopharmacol Biol Psychiatry* 2001; **25:** 1023–33.

Hypotension. SSRIs have been used in patients with neurally mediated hypotension refractory to standard treatment (see p.1174), although evidence of benefit is mainly anecdotal. However, a small study[1] found that paroxetine reduced the incidence of both tilt-induced and spontaneous syncope.

See also Orthostatic Hypotension, below.

1. Di Girolamo E, *et al.* Effects of paroxetine hydrochloride, a selective serotonin reuptake inhibitor, on refractory vasovagal syncope: a randomized, double-blind, placebo-controlled study. *J Am Coll Cardiol* 1999; **33:** 1227–30.

Obesity. Fluoxetine has been tried with some success as part of the management of obesity (p.2149). Fluoxetine's mechanism of action in obesity is unknown. Serotonin is believed to be involved in the regulation of satiety[1] but fluoxetine has also been shown to increase resting energy expenditure and raise basal body temperature.[2] A common dose for fluoxetine in the management of obesity has been 60 mg daily; it appears that fluoxetine has a dose-related effect on weight loss.[3] Reviews[1,4,5] agree that fluoxetine can aid weight reduction in the short term but after 16 to 20 weeks some patients have started to regain weight and its long-term efficacy remains to be established. Troublesome adverse effects can occur.[1] Some patients treated with fluoxetine for depression have experienced an increase of appetite and some have gained weight. There has been a report[6] of a patient who lost weight during treatment with fluoxetine for depression despite an increased appetite and food intake.

1. Anonymous. Fluoxetine (Prozac) and other drugs for treatment of obesity. *Med Lett Drugs Ther* 1994; **36:** 107–8.
2. Bross R, Hoffer LJ. Fluoxetine increases resting energy expenditure and basal body temperature in humans. *Am J Clin Nutr* 1995; **61:** 1020–5.
3. Levine LR, *et al.* Use of fluoxetine, a selective serotonin-uptake inhibitor, in the treatment of obesity: a dose-response study. *Int J Obes* 1989; **13:** 635–45.
4. Bray GA. Use and abuse of appetite-suppressant drugs in the treatment of obesity. *Ann Intern Med* 1993; **119:** 707–13.
5. Mayer LE, Walsh BT. The use of selective serotonin reuptake inhibitors in eating disorders. *J Clin Psychiatry* 1998; **59** (suppl 15): 28–34.
6. Fichtner CG, Braun BG. Hyperphagia and weight loss during fluoxetine treatment. *Ann Pharmacother* 1994; **28:** 1350–2.

Orthostatic hypotension. Although orthostatic hypotension has been reported in some patients taking SSRIs, there has been a report[1] that fluoxetine 20 mg daily for 6 to 8 weeks produced beneficial effects in 4 of 5 patients with chronic symptomatic orthostatic hypotension (p.1530) refractory to other treatment. Modest benefits have also been seen in patients with orthostatic hypotension associated with parkinsonism.[2]

1. Grubb BP, *et al.* Fluoxetine hydrochloride for the treatment of severe refractory orthostatic hypotension. *Am J Med* 1994; **97:** 366–8.
2. Montastruc JL, *et al.* Fluoxetine in orthostatic hypotension of Parkinson's disease: a clinical and experimental pilot study. *Fundam Clin Pharmacol* 1998; **12:** 398–402.

Pain. SSRIs have been tried in the treatment of painful disorders including fibromyalgia and diabetic neuropathy.

See also Headache, above.

References.

1. Goldenberg D, *et al.* A randomized, double-blind crossover trial of fluoxetine and amitriptyline in the treatment of fibromyalgia. *Arthritis Rheum* 1996; **39:** 1852–9.
2. Jung AC, *et al.* The efficacy of selective serotonin reuptake inhibitors for the management of chronic pain. *J Gen Intern Med* 1997; **12:** 384–9.
3. Smith AJ. The analgesic effects of selective serotonin reuptake inhibitors. *J Psychopharmacol* 1998; **12:** 407–13.
4. Anderberg UM, *et al.* Citalopram in patients with fibromyalgia–a randomized, double-blind, placebo-controlled study. *Eur J Pain* 2000; **4:** 27–35.
5. Shimodozono M, *et al.* Reduction of central poststroke pain with the selective serotonin reuptake inhibitor fluvoxamine. *Int J Neurosci* 2002; **112:** 1173–81.
6. Arnold LM, *et al.* A randomized, placebo-controlled, double-blind, flexible-dose study of fluoxetine in the treatment of women with fibromyalgia. *Am J Med* 2002; **112:** 191–7.

Parkinsonism. It has been suggested that fluoxetine might be of use in the management of selected patients with Parkinson's disease (p.791) who have levodopa-induced dyskinesias unresponsive to other measures.[1] However, although fluoxetine has been reported to have produced beneficial results in such patients[2] there has also been a report of increased disability in patients with Parkinson's disease given fluoxetine.[3] Extrapyramidal effects have also been reported in other patients taking fluoxetine (see under Adverse Effects, above). Fluoxetine has been tried in parkinsonism-related orthostatic hypotension (above).

1. Giron LT, Koller WC. Methods of managing levodopa-induced dyskinesias. *Drug Safety* 1996; **14:** 365–74.
2. Durif F, *et al.* Levodopa-induced dyskinesias are improved by fluoxetine. *Neurology* 1995; **45:** 1855–8.
3. Steur ENHJ. Increase of Parkinson disability after fluoxetine medication. *Neurology* 1993; **43:** 211–3.

Pathological crying or laughing. Inappropriate or uncontrolled crying or laughing can occur in patients with lesions in certain areas of the brain. Attempts at treatment have mostly been with antidepressant drugs, including SSRIs. Beneficial effects have been claimed for fluoxetine in a number of uncontrolled studies and reports.[1-4]

1. Seliger GM, *et al.* Fluoxetine improves emotional incontinence. *Brain Inj* 1992; **6:** 267–70.
2. Sloan RL, *et al.* Fluoxetine as a treatment for emotional lability after brain injury. *Brain Inj* 1992; **6:** 315–19.
3. Hanger HC. Emotionalism after stroke. *Lancet* 1993; **342:** 1235–6.
4. Tsai WC, *et al.* Treatment of emotionalism with fluoxetine during rehabilitation. *Scand J Rehabil Med* 1998; **30:** 145–9.

Peripheral vascular disease. Anecdotal reports[1,2] and a small pilot study[3] of fluoxetine (in a daily dose of 20 to 60 mg) suggest it may produce favourable therapeutic responses in patients with Raynaud's syndrome (see Vasospastic Arterial Disorders, p.1188).

1. Bolte MA, Avery D. Case of fluoxetine-induced remission of Raynaud's phenomenon—a case report. *Angiology* 1993; **44:** 161–3.
2. Jaffe IA. Serotonin reuptake inhibitors in Raynaud's phenomenon. *Lancet* 1995; **345:** 1378.
3. Coleiro B, *et al.* Treatment of Raynaud's phenomenon with the selective serotonin reuptake inhibitor fluoxetine. *Rheumatology (Oxford)* 2001; **40:** 1038–43.

Premenstrual syndrome. Fluoxetine is used to control both the psychological and somatic symptoms of women with premenstrual dysphoric syndrome, a severe form of premenstrual syndrome (p.2099). Other SSRIs also appear to be useful, although evidence is so far more limited.

References.

1. Romano S, *et al.* The role of fluoxetine in the treatment of premenstrual dysphoric disorder. *Clin Ther* 1999; **21:** 615–33.
2. Eriksson E. Serotonin reuptake inhibitors for the treatment of premenstrual dysphoria. *Int Clin Psychopharmacol* 1999; **14** (suppl 2): S27–S33.
3. Dimmock PW, *et al.* Efficacy of selective serotonin-reuptake inhibitors in premenstrual syndrome: a systematic review. *Lancet* 2000; **356:** 1131–6.
4. Carr RR, Ensom MHH. Fluoxetine in the treatment of premenstrual dysphoric disorder. *Ann Pharmacother* 2002; **36:** 713–17.
5. Pearlstein T. Selective serotonin reuptake inhibitors for premenstrual dysphoric disorder: the emerging gold standard. *Drugs* 2002; **62:** 1869–85.
6. Wyatt KM, *et al.* Selective serotonin reuptake inhibitors for premenstrual syndrome. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2002 (accessed 24/11/05).
7. Luisi AF, Pawasauskas JE. Treatment of premenstrual dysphoric disorder with selective serotonin reuptake inhibitors. *Pharmacotherapy* 2003; **23:** 1131–40.

Sexual dysfunction. Impotence or ejaculatory problems have been reported as adverse effects of SSRIs (see Effects on Sexual Function in Adverse Effects, above). Such properties of the SSRIs have been studied as a potential form of treatment for men with premature ejaculation[1-3] (p.2181). The relative effects of the SSRIs on delaying ejaculation have also been studied.[4] Paroxetine was found to cause the strongest delay, followed by fluoxetine and then sertraline; fluvoxamine caused a slight delay although the effect was not significantly different from that seen with placebo. (Citalopram was unavailable at the time of the study; later studies of its effect have been conflicting[3].)

1. Waldinger MD, *et al.* Paroxetine treatment of premature ejaculation: a double-blind, randomized, placebo-controlled study. *Am J Psychiatry* 1994; **151:** 1377–9.
2. Mendels J, *et al.* Sertraline treatment for premature ejaculation. *J Clin Psychopharmacol* 1995; **15:** 341–6.
3. Moreland AJ, Makela EH. Selective serotonin-reuptake inhibitors in the treatment of premature ejaculation. *Ann Pharmacother* 2005; **39:** 1296–1301.
4. Waldinger MD, *et al.* Effect of SSRI antidepressants on ejaculation: a double-blind, randomized, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine and sertraline. *J Clin Psychopharmacol* 1998; **18:** 274–81.

Preparations

BP 2008: Fluoxetine Capsules; Fluoxetine Oral Solution;
USP 31: Fluoxetine Capsules; Fluoxetine Delayed-Release Capsules; Fluoxetine Oral Solution; Fluoxetine Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Alental; Animex-On; Anzolden; Captaton; Eburnate; Equilibrane; Faboxetina; Felixina; Fibrotina; Fluopiram; Foxetin; Lapsus; Mitilase; Nervosal; Neupax; Neuro Laz; Prozac; Saurat; ***Austral.:*** Auscap; Erocap†; Fluohexal; Fluoxebell; Lovan; Prozac; Zactin; ***Austria:*** Felicium; Fluctine; Fluoxenorm; Fluoxibene; Fluoxistad; Fluoxityrol†; Flux; Fluxil; FluxoMed; Mutan; NuFluo; Positivum; ***Belg.:*** Docfluoxetine; Fluox; Fluoxemed; Fluoxone; Fontex; Prosimed; Prozac; ***Braz.:*** Daforin; Deprax; Depress; Eufor; Fluox; Fluxene; Nortec; Prozac; Prozen; Psiquial; Verotina; ***Canad.:*** FXT; Prozac; ***Chile:*** Actan; Alentol; Anisimol; Clinium; Dominium; Pragmaten; Prozac; Sostac; Tremafarm†; ***Cz.:*** Deprenon†; Deprex; Floxet; Flumirex†; Fluocim†; Fluogal†; Fluoxin; Fluval†; Fluxonil†; Fluzak; Framex†; Magrilan; Milezin†; Portal; Prozac; ***Denm.:*** Afeksin; Flutin; Fluxantin†; Folizol; Fondur†; Fonigen†; Fontex; Fonzac; ***Fin.:*** Fluoxal†; Fluxantin†; Fontex†; Seromex; Seronil; ***Fr.:*** Prozac; ***Ger.:*** Fluctin; Fluneurin; Fluox; Fluox-Puren; Fluoxa†; Fluoxe-Q; FluoxeLich; Fluoxemerck†; Fluoxgamma; Fluxet; Fysionorm†; ***Gr.:*** Dagrilan; Dinalexin; Exostrept; Flonital; Fluocalm; Fluxadir; Fokeston; Hapilux; Ladose; Orthon; Sartuzin; Sofelin; Stephadilat-S; Stressless; Thiramil; Zinovat; ***Hong Kong:*** Atd; CP-Fluoxet; Deprexin; Fluxetin; Fluxil; Magrilan†; Nopres; Plazeron†; Provatine†; Prozac; Qualisac; ***Hung.:*** Deprexin; Fefluzin†; Floxet; FluWinox; Portal; Prozac; ***India:*** Depzac; Fludac; Flufran†; Nuzac; Platin; ***Indon.:*** Andep; Ansi; Antiprestin; Courage; Elizac; Kalxetin; Lodep; Nopres; Noxetine; Oxipres; Prozac; ZAC; Zactin; ***Irl.:*** Affex; Biozac; Gerozac; Norzac; Prozac; Prozamel; Prozatan; Prozit; ***Israel:*** Affectine; Flutine; Prizma; Prozac; ***Ital.:*** Azur; Clexiclor; Cloriflox; Deprexen; Diesan; Flotina; Fluoxeren; Fluoxin†; Grinflux†; Ibixetin†; Ipsumor; Prozac; Serezac†; Xeredien; Zafluox†; ***Malaysia:*** Fluran; Fluxetil; Prozac; Salipax; ***Mex.:*** Aponeusak†; Auroken†; Axtin; Deprozin; Farmaxetina; Flocet; Florexal; Fluctine; Fluneurin; Fluoxac; Fluralex; Flutinax; Indozul; Lebensart; Ovisen; Prozac; Quanilene; Regultron; Siquial; Ulmely; Zatin; ***Neth.:*** Fluoxstad; Flustad; Prozac; ***Norw.:*** Fontex; ***NZ:*** Fluox; Plinzene; Prozac; ***Philipp.:*** Adepssir; Deprexone; Deprizac; Prozac; ***Pol.:*** Andepin; Bioxetin; Deprexetin; Salipax; Seronil; ***Port.:*** Digassim; Mizac†; Nodepe†; Prozac; Psipax; Salipax; Selectus; Tuneluz; ***Rus.:*** Apo-Fluoxetine (Апо-Флуоксетин); Fluval (Флувал); Framex (Фрамекс); Portal (Портал); Prodep (Продеп); Proflusak (Профлузак); Prozac (Прозак); ***S.Afr.:*** Deprozan; Lorien; Nuzak; Prohexal; Prozac; Ranflocs; Sanzur†; ***Singapore:*** Deprexin; Fluxetil†; Fluxetin; Fluxil; Foxtin; Magrilan; Prozac; Zactin; ***Spain:*** Adofen; Astrin†; Augort†; Lecimar; Luramon; Nodepe; Prozac; Reneuron; Zaxetina†; ***Swed.:*** Fluxantin†; Fontex; Seroscand†; ***Switz.:*** Fluctine; Fluesco; Fluocim; fluox-basan†; Fluoxifar; Flusol; ***Thai.:*** Actisac†; Anzac; Atd†; Dawnex; Deproxin; Flulox; Flumed; Fluoxine; Flusac; Flutine; Fluxetil; Fluxetin; Fluzac; Hapilux†; Loxetine; Magrilan; Oxetine; Oxsac; Prodep; Prozac; Unprozy; ***Turk.:*** Depreks; Fulsac; Loksetin; Prozac; Seronil; Zedprex; ***UAE:*** Flutin; ***UK:*** Prozac; Prozit; ***USA:*** Prozac; Sarafem; ***Venez.:*** Anoxen; Antipres; Fluxet; Fluzac; Prozac; Psiquial.

Multi-ingredient: ***Arg.:*** Combined†; Symbyax†; ***Chile:*** Symbyax; ***India:*** Fludep Plus; ***Mex.:*** Symbyax; ***USA:*** Symbyax.

Fluvoxamine Maleate *(BANM, USAN, rINNM)*

DU-23000; Fluvoksamiinimaleaatti; Fluvoksamin Maleat; Fluvoxamine, maléate de; Fluvoxamini maleas; Fluvoxaminmaleat; Maleato de fluvoxamina. (*E*)-5-Methoxy-4′-trifluoromethylvalerophenone *O*-2-aminoethyloxime maleate.

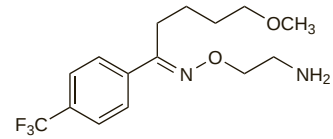
Флувоксамина Малеат

$C_{15}H_{21}F_3N_2O_2,C_4H_4O_4$ = 434.4.

CAS — 54739-18-3 (fluvoxamine); 61718-82-9 (fluvoxamine maleate).

ATC — N06AB08.

ATC Vet — QN06AB08.



(fluvoxamine)

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

Ph. Eur. 6.2 (Fluvoxamine Maleate). A white or almost white, crystalline powder. Sparingly soluble in water; freely soluble in alcohol and in methyl alcohol.

USP 31 (Fluvoxamine Maleate). A white to off-white, crystalline powder. Sparingly soluble in water; freely soluble in alcohol and in chloroform; practically insoluble in solvent ether. Protect from light.

Adverse Effects, Treatment, and Precautions

As for SSRIs in general (see Fluoxetine, p.391).

Bradycardia with ECG changes has been noted with fluvoxamine (but see also Effects on the Cardiovascular System in Adverse Effects of Fluoxetine, p.392).

It is recommended that fluvoxamine should be withdrawn in patients who have increased serum liver enzyme concentrations.

Fluvoxamine may need to be given with caution to patients with hepatic or renal impairment, and to the elderly (see under Uses and Administration, below).

Incidence of adverse effects. The UK CSM has reported[1] that between 25 September 1986 and 23 March 1988 it had received 961 reports of adverse reactions, including 5 deaths, associated with the use of fluvoxamine. The most frequently reported reactions were nausea (183) and vomiting (101). Other reactions included dizziness, somnolence, agitation, headache, tremor, and, during the first few days, worsening of anxiety. There were 13 reports of convulsions. Reports of appetite stimulation and antimuscarinic reactions were unusual. The effects sometimes resolved with time or dose reduction.

The safety profile of fluvoxamine has been reviewed.[2] For a comparison of the adverse reaction profiles of other SSRIs including fluoxetine with that of fluvoxamine, see Incidence of Adverse Effects, under Adverse Effects of Fluoxetine, p.391.

1. CSM. Fluvoxamine (Faverin): adverse reaction profile. *Current Problems 22* 1988. Also available at: http:// www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024429&RevisionSelectionMethod=LatestReleased (accessed 04/08/08)
2. Wagner W, *et al.* Fluvoxamine: a review of its safety profile in world-wide studies. *Int Clin Psychopharmacol* 1994; **9:** 223–7.

Breast feeding. For comments on the use of SSRIs in breast feeding patients, see under Precautions for Fluoxetine, p.394.

Children. SSRIs are associated with an increased risk of potentially suicidal behaviour when used for the treatment of depression in children and adolescents under 18 years old; for further details, see under Effects on Mental State in Fluoxetine, p.392.

Interactions

For interactions associated with SSRIs, see Fluoxetine, p.396.

Fluvoxamine can greatly increase plasma concentrations of theophylline (see p.1143), and they should not be given together, or, if this is unavoidable, the dose of theophylline should be halved and plasma-theophylline concentrations monitored more closely.

◊ References.

1. Wagner W, Vause EW. Fluvoxamine: a review of global drug-drug interaction data. *Clin Pharmacokinet* 1995; **29** (suppl 1): 26–32.

Pharmacokinetics

Fluvoxamine is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring 3 to 8 hours after a dose. Systemic bioavailability does not appear to be affected by food. It is extensively metabolised in the liver by oxidative demethylation and deamination, to inactive metabolites. Excretion is mainly in the urine; about 2% of a dose is excreted as unchanged drug. Fluvoxamine is widely distributed throughout the body and protein binding is reported to be about 80%; it has a plasma-elimination half-life of about 15 hours. Fluvoxamine is distributed into breast milk (see Breast Feeding under Precautions in Fluoxetine, p.394).

◊ References.

1. Perucca E, *et al*. Clinical pharmacokinetics of fluvoxamine. *Clin Pharmacokinet* 1994; **27:** 175–90.
2. van Harten J. Overview of the pharmacokinetics of fluvoxamine. *Clin Pharmacokinet* 1995; **29** (suppl 1): 1–9.
3. Xu Z-H, *et al*. In vivo inhibition of CYP2C19 but not CYP2D6 by fluvoxamine. *Br J Clin Pharmacol* 1996; **42:** 518–21.
4. DeVane CL, Gill HS. Clinical pharmacokinetics of fluvoxamine: applications to dosage regimen design. *J Clin Psychiatry* 1997; **58** (suppl 5): 7–14.
5. Spigset O, *et al*. Non-linear fluvoxamine disposition. *Br J Clin Pharmacol* 1998; **45:** 257–63.
6. Hiemke C, Härtter S. Pharmacokinetics of selective serotonin re-uptake inhibitors. *Pharmacol Ther* 2000; **85:** 11–28.

Uses and Administration

Fluvoxamine, an aralkylketone derivative, is an SSRI with actions and uses similar to those of fluoxetine (p.397). It is used as the maleate and doses are expressed in terms of this salt.

In the treatment of **depression** fluvoxamine maleate is given in an initial oral dose of 50 or 100 mg once daily, preferably in the evening; in some patients the dose may need to be gradually increased to a maximum of 300 mg daily. It is recommended that daily dosages exceeding 150 mg should be given in 2 or 3 divided doses.

Fluvoxamine maleate is also used in the management of **obsessive-compulsive disorder**. In the UK, doses are similar to those used in the treatment of depression. The recommended starting dose in the USA is 50 mg once daily; this dose may be increased by increments of 50 mg every 4 to 7 days to a maximum of 300 mg daily. Doses above 100 mg daily should be given in 2 divided doses. In both countries the drug may also be used in children aged 8 years and over with obsessive-compulsive disorder. The recommended starting dose is 25 mg once daily, which may be increased in increments of 25 mg every 4 to 7 days to a maximum daily dose of 200 mg (in the USA adolescents over 11 years may be given a maximum dose of 300 mg daily). Daily doses of more than 50 mg should be given as 2 divided doses. It is recommended that if no improvement occurs within 10 weeks, treatment with fluvoxamine should be re-assessed.

In the USA, a modified-release preparation of fluvoxamine maleate is available for the treatment of obsessive-compulsive disorder and **social anxiety disorder** in adults; the initial dose is 100 mg once daily increased, as necessary, to a maximum of 300 mg once daily.

US licensed product information recommends that dosage modification be considered in elderly patients, in whom clearance may be decreased. For dosage in renal and hepatic impairment, see below.

Fluvoxamine should be withdrawn gradually to reduce the risk of withdrawal symptoms.

Administration in hepatic or renal impairment. UK licensed drug information recommends that patients with hepatic or renal impairment should begin therapy with a low dose of fluvoxamine maleate and be carefully monitored; US product information only recommends that dosage modification be considered in hepatic impairment, since it considers evidence of accumulation in renal impairment to be lacking.

Anxiety disorders. Fluvoxamine has been given in a variety of anxiety disorders including obsessive-compulsive disorder (p.952), panic disorder (p.952), and social anxiety disorder (see under Phobic Disorders, p.953).

References.

1. van Vliet IM, *et al*. Psychopharmacological treatment of social phobia: a double blind placebo controlled study with fluvoxamine. *Psychopharmacology (Berl)* 1994; **115:** 128–34.
2. Freeman CPL, *et al.* Fluvoxamine versus clomipramine in the treatment of obsessive compulsive disorder: a multicenter, randomized, double-blind, parallel group comparison. *J Clin Psychiatry* 1994; **55:** 301–5.
3. Greist JH, *et al.* Efficacy of fluvoxamine in obsessive-compulsive disorder: results of a multicentre, double blind, placebo-controlled trial. *Eur J Clin Res* 1995; **7:** 195–204.
4. Stein MB, *et al.* Fluvoxamine treatment of social phobia (social anxiety disorder): a double-blind placebo-controlled study. *Am J Psychiatry* 1999; **156:** 756–60.
5. Figgitt DP, McClellan KJ. Fluvoxamine: an updated review of its use in the management of adults with anxiety disorders. *Drugs* 2000; **60:** 925–54.
6. The Research Unit on Pediatric Psychopharmacology Anxiety Study Group. Fluvoxamine for the treatment of anxiety disorders in children and adolescents. *N Engl J Med* 2001; **344:** 1279–85.
7. Asnis GM, *et al*. Fluvoxamine in the treatment of panic disorder: a multi-center, double-blind, placebo-controlled study in outpatients. *Psychiatry Res* 2001; **103:** 1–14.
8. Hollander E, *et al.* A double-blind, placebo-controlled study of the efficacy and safety of controlled-release fluvoxamine in patients with obsessive-compulsive disorder. *J Clin Psychiatry* 2003; **64:** 640–7.
9. Stein DJ, *et al*. Fluvoxamine CR in the long-term treatment of social anxiety disorder: the 12- to 24-week extension phase of a multicentre, randomized, placebo-controlled trial. *Int J Neuropsychopharmacol* 2003; **6:** 317–23.

Hypochondriasis. For reference to the use of SSRIs, including fluvoxamine, in hypochondriasis, see under Fluoxetine, p.398.

Preparations

BP 2008: Fluvoxamine Tablets;
USP 31: Fluvoxamine Maleate Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Luvox†; ***Austral.:*** Faverin; Luvox; Movox; Voxam; ***Austria:*** Felixsan; Floxyfral; ***Belg.:*** Dumirox†; Floxyfral; ***Braz.:*** Luvox; ***Canad.:*** Luvox; ***Chile:*** Luvox; ***Cz.:*** Fevarin; ***Denm.:*** Fevarin; ***Fin.:*** Fevarin; Fluvosol†; ***Fr.:*** Floxyfral; ***Ger.:*** Desifluvoxamin†; Fevarin; Fluvohexal; Fluvoxadura; ***Gr.:*** Dumyrox; Myroxine; ***Hong Kong:*** Faverin; ***Hung.:*** Fevarin; ***India:*** Fluvoxin; Sorest; Uvox; ***Indon.:*** Luvox; ***Irl.:*** Faverin; ***Israel:*** Favoxil; ***Ital.:*** Dumirox; Fevarin; Maveral; ***Jpn:*** Luvox; ***Malaysia:*** Luvox; ***Mex.:*** Luvox; Vumix; ***Neth.:*** Fevarin; ***Norw.:*** Fevarin; ***Philipp.:*** Faverin; ***Pol.:*** Fevarin; ***Port.:*** Dumyrox; ***Rus.:*** Fevarin (Феварин); ***S.Afr.:*** Faverin; Luvox; ***Singapore:*** Faverin; ***Spain:*** Dumirox; ***Swed.:*** Fevarin; ***Switz.:*** Flox-ex; Floxyfral; ***Thai.:*** Faverin; Fluvoxin; ***Turk.:*** Faverin; ***UK:*** Faverin; ***USA:*** Luvox; ***Venez.:*** Luvox.

Imipramine *(BAN, rINN)*

Imipramiini; Imipramin; Imipramina; Imipraminum. 3-(10,11-Dihydro-5*H*-dibenz[*b,f*]azepin-5-yl)propyldimethylamine.

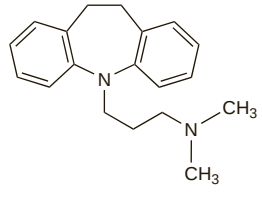
Имипрамин

$C_{19}H_{24}N_2$ = 280.4.

CAS — 50-49-7.

ATC — N06AA02.

ATC Vet — QN06AA02.



Imipramine Embonate *(BANM, rINNM)*

Embonato de imipramina; Imipramine, Embonate d'; Imipramine Pamoate; Imipramini Embonas.

Имипрамина Эмбонат

$(C_{19}H_{24}N_2)_2.C_{23}H_{16}O_6$ = 949.2.

CAS — 10075-24-8.

Imipramine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de imipramina; Imipram. Hydrochlor.; Imipramiinihydrokloridi; Imipramin Hidroklorür; Imipramine, chlorhydrate d'; Imipramin-hidroklorid; Imipramin-hydrochlorid; Imipraminhydroklorid; Imipramini Chloridum; Imipramini hydrochloridum; Imipramino hidrochloridas; Imipraminy chlorowodorek; Imizine.

Имипрамина Гидрохлорид

$C_{19}H_{24}N_2$,HCl = 316.9.

CAS — 113-52-0.

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

Ph. Eur. 6.2 (Imipramine Hydrochloride). A white or slightly yellow crystalline powder. Freely soluble in water and in alcohol. A 10% solution in water has a pH of 3.6 to 5.0. Protect from light.

USP 31 (Imipramine Hydrochloride). A white to off-white, odourless or practically odourless, crystalline powder. Freely soluble in water and in alcohol; soluble in acetone; insoluble in ether and in benzene. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for tricyclic antidepressants in general (see Amitriptyline, p.376).

Breast feeding. For comments on the use of tricyclic antidepressants in breast feeding patients, see under Precautions for Amitriptyline, p.378.

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

Interactions

For interactions associated with tricyclic antidepressants, see Amitriptyline, p.379.

Pharmacokinetics

Imipramine is readily absorbed from the gastrointestinal tract, and extensively demethylated by first-pass metabolism in the liver, to its primary active metabolite, desipramine.

Paths of metabolism of both imipramine and desipramine include hydroxylation and *N*-oxidation. Imipramine is excreted in the urine, mainly in the form of its metabolites, either free or in conjugated form; small amounts are excreted in the faeces via the bile.

Imipramine and desipramine are widely distributed throughout the body and are extensively bound to plasma and tissue protein. Imipramine has been estimated to have an elimination half-life ranging from 9 to 28 hours, which may be considerably extended in overdosage. Plasma concentrations of imipramine and desipramine vary very widely between individuals but some correlation with therapeutic response has been established.

Imipramine and desipramine cross the blood-brain barrier and placenta and are distributed into breast milk (see Breast Feeding under Precautions in Amitriptyline, p.378).

◊ References.

1. Sallee FR, Pollock BG. Clinical pharmacokinetics of imipramine and desipramine. *Clin Pharmacokinet* 1990; **18:** 346–64.

Uses and Administration

Imipramine is a dibenzazepine tricyclic antidepressant with actions and uses similar to those of amitriptyline (p.381). Imipramine is one of the less sedating tricyclics and has moderate antimuscarinic activity. Imipramine is usually given orally as the hydrochloride or embonate, with doses expressed in terms of the hydrochloride. Imipramine embonate 149.8 mg and imipramine base 88.5 mg are both equivalent to about 100 mg of imipramine hydrochloride.

In the treatment of **depression**, the usual daily dose of imipramine hydrochloride is up to 75 mg in divided doses initially, gradually increased to 150 to 200 mg daily as necessary; higher doses of up to 300 mg daily may be required in severely depressed patients in hospital. A suggested initial dose for the elderly in the UK