with tricyclic antidepressants; it also inhibits the neuronal reuptake of dopamine. The antidepressant effect may not be evident until after 4 weeks of therapy. Bupropion is also used as an aid to smoking cessation.

Bupropion is given orally as the hydrochloride. To minimise agitation, anxiety, and insomnia often experienced at the start of therapy, and to reduce the risk of seizures, doses should be increased gradually; the total daily dose should be given in equally divided doses and the maximum recommended single and total daily doses should not be exceeded. Insomnia at the start of therapy may be minimised by avoiding bedtime doses. Patients with hepatic or renal impairment should be given reduced doses and monitored for toxic effects (see below).

In the treatment of **depression** bupropion hydrochloride is given in initial doses of 100 mg twice daily increased, if necessary, after at least 3 days to 100 mg three times daily. In severe cases, if no improvement has been observed after several weeks of therapy, the dose may be increased further to a maximum of 150 mg three times daily. Bupropion hydrochloride is also available as a modified-release preparation given in an initial dose of 150 mg once daily in the morning increased, if necessary, after at least 3 days to 150 mg twice daily; in severe cases, the dose of the modified-release preparation may be increased further after several weeks to 200 mg twice daily. A modified-release preparation that is given once daily is also available; the maximum daily dose for this preparation is 450 mg as a single dose in the morning. A modified-release preparation is also licensed for the prevention of depression in patients with seasonal affective disorder; the maximum dose for this disorder is 300 mg once daily.

Bupropion hydrochloride is given as a modified-release preparation as an aid to **smoking cessation** in an initial dose of 150 mg once daily for 6 days, increasing to 150 mg twice daily on day 7. In the USA, the dose may be increased after 3 days. In the UK, the maximum recommended dose in the elderly, or in patients with predisposing risk factors for seizure (see Precautions, above), is 150 mg daily. Treatment should be started about 1 to 2 weeks before the patient attempts to stop smoking, to allow steady-state blood levels of bupropion to be reached, and normally continues for 7 to 12 weeks; if there is no significant progress towards smoking abstinence by the seventh week, then therapy should be stopped. Use with nicotine transdermal patches may be warranted in some patients, although there is a risk of hypertension with such therapy (see Interactions, above).

Administration in hepatic impairment. When used as an aid to *smoking cessation* in patients with mild to moderate hepatic impairment, bupropion should be given at a reduced frequency; UK licensed product information suggests an oral dose of 150 mg once daily. The use of bupropion in patients with severe hepatic cirrhosis is contra-indicated in the UK although doses of 150 mg every other day are permitted in the USA.

In the treatment of *depression*, a reduction in the frequency and/or the dose of bupropion should be considered in patients with mild to moderate impairment. In patients with severe hepatic cirrhosis the dose varies according to the preparation given; for modified-release bupropion the suggested maximum oral dose is 100 mg once daily or 150 mg every other day while the maximum dose of immediate-release bupropion is 75 mg once daily.

Administration in renal impairment. When used as an aid to *smoking cessation* in patients with renal impairment, bupropion should be given at a reduced frequency; UK licensed product information suggests an oral dose of 150 mg once daily.

In the treatment of *depression*, a reduction in the frequency and/or the dose of bupropion should be considered.

Depression. As discussed on p.373, there is very little difference in efficacy between the different groups of antidepressant drugs, and choice is often made on the basis of adverse effect profile. Bupropion has a different biochemical profile from both the tricyclics and the SSRIs; however, like the SSRIs, it may be safer in overdosage than the older tricyclics.

References.
1. Kavoussi RJ, *et al.* Double-blind comparison of bupropion sustained release and sertraline in depressed outpatients. *J Clin Psychiatry* 1997; **58:** 532–7.
2. Nieuwstraten CE, Dolovich LR. Bupropion versus selective serotonin-reuptake inhibitors for treatment of depression. *Ann Pharmacother* 2001; **35:** 1608–13.
3. Weihs KL, *et al.* Continuation phase treatment with bupropion SR effectively decreases the risk for relapse of depression. *Biol Psychiatry* 2002; **51:** 753–61.
4. Glod CA, *et al.* Open trial of bupropion SR in adolescent major depression. *J Child Adolesc Psychiatr Nurs* 2003; **16:** 123–30.
5. Rush AJ, *et al.* The STAR*D Study Team. Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs for depression. *N Engl J Med* 2006; **354:** 1231–42.
6. Papakostas GI, *et al.* Comparing the rapidity of response during treatment of major depressive disorder with bupropion and the SSRIs: a pooled survival analysis of 7 double-blind, randomized clinical trials. *J Clin Psychiatry* 2007; **68:** 1907–12.
7. Dhillon S, *et al.* Bupropion: a review of its use in the management of major depressive disorder. *Drugs* 2008; **68:** 653–89.

Hyperactivity. When drug therapy is indicated for attention deficit hyperactivity disorder (p.2148) initial treatment is usually with a central stimulant. Antidepressants may be used for patients who fail to respond to, or who are intolerant of, central stimulants. Data from open and controlled studies involving small numbers of patients suggest that bupropion is effective in adults and children.[1,2]

1. Cantwell DP. ADHD through the life span: the role of bupropion in treatment. *J Clin Psychiatry* 1998; **59** (suppl 4): 92–4.
2. Wilens TE, *et al.* A controlled clinical trial of bupropion for attention deficit hyperactivity disorder in adults. *Am J Psychiatry* 2001; **158:** 282–8.

Smoking cessation. Bupropion is effective in the management of smoking cessation (p.2354) and may be used as a first-line alternative to nicotine replacement therapy (NRT); its action is said to be independent of its antidepressant activity. Bupropion with NRT has also been used successfully although there is an increased risk of hypertension with this combination (see Interactions, above).

References:
1. Hurt RD, *et al.* A comparison of sustained-release bupropion and placebo for smoking cessation. *N Engl J Med* 1997; **337:** 1195–1202.
2. Jorenby DE, *et al.* A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. *N Engl J Med* 1999; **340:** 685–91.
3. Holm KJ, Spencer CM. Bupropion: a review of its use in the management of smoking cessation. *Drugs* 2000; **59:** 1007–1024.
4. Tashkin DP, *et al.* Smoking cessation in patients with chronic obstructive pulmonary disease: a double-blind, placebo-controlled, randomised trial. *Lancet* 2001; **357:** 1571–5.
5. Gonzales DH, *et al.* Bupropion SR as an aid to smoking cessation in smokers treated previously with bupropion: a randomized placebo-controlled study. *Clin Pharmacol Ther* 2001; **69:** 438–44.
6. Hays JT, *et al.* Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation: a randomized, controlled trial. *Ann Intern Med* 2001; **135:** 423–33.
7. NICE. Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation: Technology Appraisal 39 (issued March 2002). Available at: http://www.nice.org.uk/nicemedia/pdf/NiceNRT39GUIDANCE.pdf (accessed 14/08/08)
8. Ahluwalia JS, *et al.* Sustained-release bupropion for smoking cessation in African Americans: a randomized controlled trial. *JAMA* 2002; **288:** 468–74.
9. Fagerström K, *et al.* Smoking cessation treatment with sustained-release bupropion: optimising approaches to management. A seminar-in-print. *Drugs* 2002; **62** (suppl 2): 1–70.
10. Hays JT, Ebbert JO. Bupropion sustained release for treatment of tobacco dependence. *Mayo Clin Proc* 2003; **78:** 1020–4.
11. Tonnesen P, *et al.* A multicentre, randomized, double-blind, placebo-controlled, 1-year study of bupropion SR for smoking cessation. *J Intern Med* 2003; **254:** 184–92.
12. Simon JA, *et al.* Bupropion for smoking cessation: a randomized trial. *Arch Intern Med* 2004; **164:** 1797–1803.
13. Hatsukami DK, *et al.* Effects of sustained-release bupropion among persons interested in reducing but not quitting smoking. *Am J Med* 2004; **116:** 151–7.
14. Roddy E. ABC of smoking cessation: bupropion and other non-nicotine pharmacotherapies. *BMJ* 2004; **328:** 509–11.
15. Hughes JR, *et al.* Antidepressants for smoking cessation. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 14/08/08).
16. Paluck EC, *et al.* Outcomes of bupropion therapy for smoking cessation during routine clinical use. *Ann Pharmacother* 2006; **40:** 185–90.

Preparations

USP 31: Bupropion Hydrochloride Extended-Release Tablets; Bupropion Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Odranal; Wellbutrin; ***Austral.:*** Clorpax; Prexaton; Zyban; ***Austria:*** Quomem; Zyban; ***Belg.:*** Zyban; ***Braz.:*** Bup; Wellbutrin; Zetron; Zyban; ***Canad.:*** Wellbutrin; Zyban; ***Chile:*** Buxon; Dosier†; Mondrian†; Wellbutrin; ***Cz.:*** Elontril; Wellbutrin; Zyban; ***Denm.:*** Zyban; ***Fin.:*** Zyban; ***Fr.:*** Zyban; ***Ger.:*** Zyban; ***Gr.:*** Zyban; ***Hong Kong:*** Wellbutrin; Zyban; ***Hung.:*** Wellbutrin; Zyban†; ***India:*** Nicotex; Zyban; ***Irl.:*** Zyban; ***Israel:*** Zyban; ***Ital.:*** Quomem†; Zyban; ***Malaysia:*** Zyban; ***Mex.:*** Butrew; Wellbutrin; ***Neth.:*** Quomem; Zyban; Zyntabac; ***Norw.:*** Zyban; ***NZ:*** Zyban; ***Pol.:*** Zyban; ***Port.:*** Elontril; Wellbutrin; Zyban; Zyntabac; ***S.Afr.:*** Wellbutrin; Zyban; ***Singapore:*** Wellbutrin; Zyban; ***Spain:*** Quomem; Zyntabac; ***Swed.:*** Zyban; ***Switz.:*** Zyban; ***Thai.:*** Quomem; ***Turk.:*** Zyban; ***UK:*** Zyban; ***USA:*** Budeprion; Wellbutrin; Zyban; ***Venez.:*** Wellbutrin; Zyban†.

Citalopram *(BAN, rINN)*

Citalopramum; Lu-10-171; Sitalopraami. 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile.

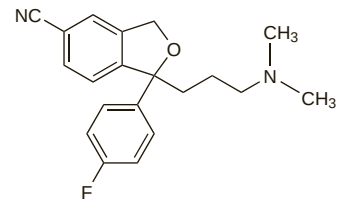
Циталопрам

$C_{20}H_{21}FN_2O$ = 324.4.

CAS — 59729-33-8.

ATC — N06AB04.

ATC Vet — QN06AB04.



Citalopram Hydrobromide *(BANM, USAN, rINNM)*

Citalopram, bromhydrate de; Citaloprami hydrobromidum; Hidrobromuro de citalopram; Lu-10-171B; Nitalapram Hydrobromide; Sitalopram Hidrobromür.

Циталопрама Гидробромид

$C_{20}H_{21}FN_2O,HBr$ = 405.3.

CAS — 59729-32-7.

Pharmacopoeias. In *US.*
USP 31 (Citalopram Hydrobromide). A white to almost white, crystalline powder. Freely soluble in water, in alcohol, and in chloroform. A 0.5% solution in water has a pH of 5.5 to 6.5.

Citalopram Hydrochloride *(BANM, rINNM)*

Citalopram, chlorhydrate de; Citaloprami hydrochloridum; Hidrocloruro de citalopram.

Циталопрама Гидрохлорид

$C_{20}H_{21}FN_2O,HCl$ = 360.9.

Adverse Effects, Treatment, and Precautions

As for SSRIs in general (see Fluoxetine, p.391) although increased appetite and weight gain have also been reported with citalopram. Citalopram may be more cardiotoxic in overdosage than other SSRIs; for further details, see p.394.

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.

Pharmacokinetics

Citalopram is readily absorbed from the gastrointestinal tract and maximum plasma concentrations are reached 2 to 4 hours after oral doses. Citalopram is widely distributed throughout the body; protein binding is less than 80%. Citalopram is metabolised by demethylation, deamination, and oxidation to active and inactive metabolites. The demethylation of citalopram to one of its active metabolites, demethylcitalopram, involves the cytochrome P450 isoenzymes CYP3A4 and CYP2C19; the metabolism of citalopram is also partly dependent on CYP2D6. Didemethylcitalopram has also been identified as a metabolite of citalopram. The elimination half-life of citalopram is reported to be about 36 hours. It is excreted mainly via the liver (85%) with the remainder via the kidneys. About 12% of the daily dose is excreted in the urine as unchanged drug. Citalopram is distributed into breast milk in very low concentrations (see Breast Feeding under Precautions in Fluoxetine, p.394).

Uses and Administration

Citalopram, a phthalane derivative, is an SSRI with actions and uses similar to those of fluoxetine (p.397). Citalopram is given orally as the hydrobromide or hydrochloride, usually as a single daily dose. Doses are expressed in terms of citalopram; citalopram hydrobromide 25.0 mg and citalopram hydrochloride 22.3 mg are each equivalent to about 20.0 mg of citalopram.

In the treatment of **depression**, the initial dose (given as tablets or a liquid) is the equivalent of 20 mg daily by mouth. After at least one week, the dose may be increased to 40 mg daily; a dose of 60 mg daily may be necessary in some patients. In the UK citalopram is also given as the hydrochloride in the form of concentrated oral drops containing the equivalent of 40 mg/mL of citalopram. The bioavailability of the drops is about 25% greater than that of the tablets and consequently daily doses appear to be lower: a 20-mg tablet dose is equivalent to a 16-mg (8 drops) dose of the concentrate. In some countries, citalopram hydrochloride has also been given by intravenous infusion in doses of 20 to 40 mg when the oral route is impracticable.

In the treatment of **panic disorder** with or without agoraphobia, the initial oral dose is 10 mg (or the equivalent as the concentrate) daily increasing to 20 mg daily after one week. The dose may be increased thereafter as required up to a maximum of 60 mg daily. In some countries citalopram is also used in the treatment of **obsessive-compulsive disorder** in doses similar to those used in depression (see above).

A dose of 20 mg daily, up to a maximum of 40 mg (or their equivalents as the concentrate), should be used in elderly patients. For dosage in hepatic and renal impairment see below.

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

The *S*-enantiomer of citalopram, escitalopram (p.391) is given for the treatment of depression and some anxiety disorders.

◊ Reviews.

1. Milne RJ, Goa KL. Citalopram: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in depressive illness. *Drugs* 1991; **41**: 450–77.

Administration in hepatic or renal impairment. Licensed drug information suggests that dosage of citalopram should be restricted to the lower end of the dose range in patients with hepatic impairment. A usual oral dose for depression in this group would be 20 mg daily although the dose may be increased up to 40 mg daily, if necessary.

There is no need for dose adjustment in mild to moderate renal impairment although information is lacking on appropriate dosage in severe impairment.

Anxiety disorders. Citalopram has been given in anxiety disorders (p.952) including panic disorder (p.952), obsessive-compulsive disorder (p.952), post-traumatic stress disorder (p.953), and social anxiety disorder (see under Phobic Disorders, p.953).

References.

1. Bouwer C, Skin DJ. Use of the selective serotonin reuptake inhibitor citalopram in the treatment of generalized social phobia. *J Affect Disord* 1998; **49:** 79–82.
2. Lepola UM, *et al.* A controlled, prospective, 1-year trial of citalopram in the treatment of panic disorder. *J Clin Psychiatry* 1998; **59:** 528–34.
3. Seedat S, *et al.* Open trial of citalopram in adults with post-traumatic stress disorder. *Int J Neuropsychopharmacol* 2000; **3:** 135–40.
4. Montgomery SA, *et al.* Citalopram 20 mg, 40 mg and 60 mg are all effective and well tolerated compared with placebo in obsessive-compulsive disorder. *Int Clin Psychopharmacol* 2001; **16:** 75–86.
5. Perna G, *et al.* A comparison of citalopram and paroxetine in the treatment of panic disorder: a randomized, single-blind study. *Pharmacopsychiatry* 2001; **34:** 85–90.
6. Marazziti D, *et al.* Citalopram in refractory obsessive-compulsive disorder: an open study. *Int Clin Psychopharmacol* 2001; **16:** 215–19.
7. Atmaca M, *et al.* Efficacy of citalopram and moclobemide in patients with social phobia: some preliminary findings. *Hum Psychopharmacol* 2002; **17:** 401–5.
8. Varia I, Rauscher F. Treatment of generalized anxiety disorder with citalopram. *Int Clin Psychopharmacol* 2002; **17:** 103–7.
9. Mukaddes NM, *et al.* Citalopram treatment of children and adolescents with obsessive-compulsive disorder: a preliminary report. *Psychiatry Clin Neurosci* 2003; **57:** 405–8.
10. Lenze EJ, *et al.* Efficacy and tolerability of citalopram in the treatment of late-life anxiety disorders: results from an 8-week randomized, placebo-controlled trial. *Am J Psychiatry* 2005; **162:** 146–50.

Depression. As discussed on p.373, there is very little difference in efficacy between the different groups of antidepressant drugs. SSRIs such as citalopram are widely used as an alternative to the older tricyclics as they have fewer adverse effects and are safer in overdosage.

References.

1. Montgomery SA, *et al.* The optimal dosing regimen for citalopram—a meta-analysis of nine placebo-controlled studies. *Int Clin Psychopharmacol* 1994; **9** (suppl 1): 35–40.
2. Keller MB. Citalopram therapy for depression: a review of 10 years of European experience and data from US trials. *J Clin Psychiatry* 2000; **61:** 896–908.
3. Parker NG, Brown CS. Citalopram in the treatment of depression. *Ann Pharmacother* 2000; **34:** 761–71.
4. Guelfi JD, *et al.* Efficacy of intravenous citalopram compared with oral citalopram for severe depression. Safety and efficacy data from a double-blind, double-dummy trial. *J Affect Disord* 2000; **58:** 201–9.
5. Hochstrasser B, *et al.* Prophylactic effect of citalopram in unipolar, recurrent depression: placebo-controlled study of maintenance therapy. *Br J Psychiatry* 2001; **178:** 304–10.
6. Klysner R, *et al.* Efficacy of citalopram in the prevention of recurrent depression in elderly patients: placebo-controlled study of maintenance therapy. *Br J Psychiatry* 2002; **181:** 29–35.
7. Roose SP, *et al.* Antidepressant pharmacotherapy in the treatment of depression in the very old: a randomized, placebo-controlled trial. *Am J Psychiatry* 2004; **161:** 2050–9.
8. Trivedi MH, *et al.* The STAR*D Study Team. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. *Am J Psychiatry* 2006; **163:** 28–40.

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. Favourable results with citalopram have been reported in a double-blind placebo-controlled study[1] and in case reports.[2,3]

1. Andersen G, *et al.* Citalopram for post-stroke pathological crying. *Lancet* 1993; **342:** 837–9.
2. Andersen G, *et al.* Citalopram treatment of traumatic brain damage in a 6-year-old boy. *J Neurotrauma* 1999; **16:** 341–4.
3. Kaschka WP, *et al.* Treatment of pathological crying with citalopram. *Pharmacopsychiatry* 2001; **34:** 254–8.

Schizophrenia. The treatment of schizophrenia consists mainly of a combination of social therapy and antipsychotic drugs (see p.955). Like other antidepressants, citalopram has been examined for its potential value as an adjuvant in schizophrenia.[1-4] In a preliminary placebo-controlled study[1] in 15 patients with chronic schizophrenia who exhibited signs of impulsive aggression, adding citalopram to existing antipsychotic therapy significantly reduced the frequency, but not the average severity, of aggressive incidents. In a subsequent study involving 90 patients, citalopram appeared to improve subjective well-being but had no clear effect on psychopathological symptoms.[2]

1. Vartiainen H, *et al.* Citalopram, a selective serotonin reuptake inhibitor, in the treatment of aggression in schizophrenia. *Acta Psychiatr Scand* 1995; **91:** 348–51.
2. Salokangas RKR, *et al.* Citalopram as an adjuvant in chronic schizophrenia: a double-blind placebo-controlled study. *Acta Psychiatr Scand* 1996; **94:** 175–80.
3. Taiminen TJ, *et al.* Citalopram as an adjuvant in schizophrenia: further evidence for a serotonergic dimension in schizophrenia. *Int Clin Psychopharmacol* 1997; **12:** 31–5.
4. Kasckow JW, *et al.* Citalopram augmentation of antipsychotic treatment in older schizophrenia patients. *Int J Geriatr Psychiatry* 2001; **16:** 1163–7.

Sexual dysfunction. SSRIs have been tried in the treatment of premature ejaculation, but results with citalopram have been conflicting, see under Fluoxetine, p.399.

Preparations

USP 31: Citalopram Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Humorap; Psiconor; Seropram; Zentius; ***Austral.:*** Celapram; Ciazil; Cipramil; Talam; Talohexal; ***Austria:*** Apertia†; Cipram†; Citalhexal†; Citalon†; Citalostad; Citarcana; Citor; Eostar; Pram; Sepram†; Seropram; ***Belg.:*** Cipramil; ***Braz.:*** Alcytam; Cipramil; Citta; Denyl; Procimax; ***Canad.:*** Celexa; ***Chile:*** Actipram; Cimal; Cipramil; Cortran; Finap; Pramcil; Prisma; Semax†; Setronil; Temperax; Zebrak; Zentius; ***Cz.:*** Apertia†; Apo-Cital; Cerotor; Cipram; Cita; Citalec; Citalon; Citaratio; Dalsan; Pram; Sepram†; Seropram; Zyloram; ***Denm.:*** Akarin; Cipramil; Citadur; Citaham; ***Fin.:*** Cipramil; Emocal†; Sepram; ***Fr.:*** Seropram; ***Ger.:*** Cilex†; Cipramil; Citadura; CitaLich; Citalo-Q; Citalon; Sepram†; Serital; ***Gr.:*** A-Depress-Therapy; Acelopram; Atinorm; Bibien; Celius; Cilopress; Cinapen; Cipram; Erlicon; Espinal; Goldamit; Lodeprem; Lopracil; Lopraxer; Malicon; Pralotam; Prefucet; Pricital; Ropramin; Selon; Seproc; Seretover; Seropram; Seror; Siloam; Sotovon; Talopram; Talopron; Taprocil; Tasonade; Verus; Vesema; Xadorek; Zanipram; ***Hong Kong:*** Cipram; Cital; ***Hung.:*** Citagen; Citalodep; Citalon; Citalowin; Citapram; Dalsan; Oropram; Seropram; Serotor; Zyloram; ***India:*** Citadep; Citopam; ***Indon.:*** Cipram; ***Irl.:*** Ciprager; Cipramil; Ciprapine; Ciprotan; Citrol; ***Israel:*** Cipramil; Recital; ***Ital.:*** Elopram; Felipram; Feliximir; Frimaind; Kaidor; Lampopram; Marpram; Percital; Pramexyl; Ricap; Seropram; Verisan; ***Malaysia:*** Cipram; ***Mex.:*** Citox; Seropram; Xylorane; ***Neth.:*** Cipramil; Ciprapine; Lontax; ***Norw.:*** Cipramil; Desital†; ***NZ:*** Celapram; Cipramil; ***Philipp.:*** Lupram; ***Pol.:*** Aurex; Cilon; Cipramil; Cital; Citaratio; Citaxin; ***Rus.:*** Cipramil (Ципрамил); Citol (Цитол); Opra (Опра); Pram (Прам); ***S.Afr.:*** Adco-Talomil; Cilift; Cipramil; CitaloHexal; Depramil; Talomil†; ***Singapore:*** Cipram; ***Spain:*** Citalvir; Genprol; Presar; Prisdal; Relapaz; Seropram; Somac; ***Swed.:*** Cipramil; Citavie; ***Switz.:*** Alutan; Claropram; Rudopram; Seropram; ***Thai.:*** Cipram; ***Turk.:*** Cipram; Citara; Citol; Citolap; ***UK:*** Cipramil; ***USA:*** Celexa; ***Venez.:*** Seropram.

Clomipramine Hydrochloride

(BANM, USAN, rINNM)

Chlorimipramine Hydrochloride; Clomipramine, chlorhydrate de; Clomipramini hydrochloridum; G-34586; Hidrocloruro de clomipramina; Klomipramiinihydrokloridi; Klomipramin Hidroklorür; Klomipramin hydrochlorid; Klomipramin-hidroklorid; Klomipraminhydroklorid; Klomipramino hidrochloridas; Monochlorimipramine Hydrochloride. 3-(3-Chloro-10,11-dihydro-5*H*-dibenz[*b,f*]azepin-5-yl)propyldimethylamine hydrochloride.

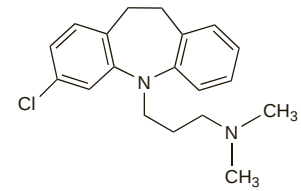
Кломипрамина Гидрохлорид

$C_{19}H_{23}ClN_2,HCl$ = 351.3.

CAS — 303-49-1 (clomipramine); 17321-77-6 (clomipramine hydrochloride).

ATC — N06AA04.

ATC Vet — QN06AA04.



(clomipramine)

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

Ph. Eur. 6.2 (Clomipramine Hydrochloride). A white or slightly yellow, slightly hygroscopic, crystalline powder. Freely soluble in water and in dichloromethane; soluble in alcohol. A 10% solution in water has a pH of 3.5 to 5.0. Protect from light.

USP 31 (Clomipramine Hydrochloride). A white to faintly yellow crystalline powder. Very soluble in water. pH of a 10% solution in water is between 3.5 and 5.0.

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. Clomipramine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems, although there is conflicting evidence of porphyrinogenicity.

Interactions

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

MAOIs. The combination of clomipramine and *tranylcypromine* is considered particularly hazardous.

The serotonin syndrome (p.416) has occurred in patients receiving clomipramine and *moclobemide* (see under Interactions of Antidepressants in Phenelzine, p.418).

Pharmacokinetics

Clomipramine is readily absorbed from the gastrointestinal tract, and extensively demethylated during first-pass metabolism in the liver to its primary active metabolite, desmethylclomipramine.

Clomipramine and desmethylclomipramine are widely distributed throughout the body and are extensively bound to plasma and tissue protein. Clomipramine has been estimated to have a plasma elimination half-life of about 21 hours, which may be considerably extended in overdosage; that of desmethylclomipramine is longer (about 36 hours).

Paths of metabolism of both clomipramine and desmethylclomipramine include hydroxylation and *N*-oxidation. About two-thirds of a single dose of clomipramine is excreted in the urine, mainly in the form of its metabolites, either free or in conjugated form; the remainder of the dose is excreted in the faeces. Clomipramine crosses the placenta and is distributed into breast milk.

◊ References.

1. Gex-Fabry M, *et al.* Clomipramine metabolism: model-based analysis of variability factors from drug monitoring data. *Clin Pharmacokinet* 1990; **19:** 241–55.