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.

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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]

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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).

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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).
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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.

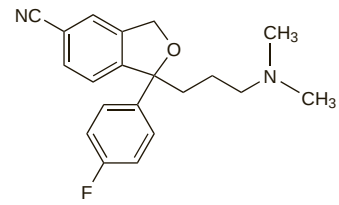
Циталопрам

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