Escitalopram Oxalate

(BANM, USAN, rINNM)

S-Citalopram Oxalate; Escitalopram, Oxalate d'; Escitalopramі Oxalas; Lu-26-054/0; Oxalato de escitalopram. (+)-(*S*)-1-[3-(dimethylamino)propyl]-1-(*p*-fluorophenyl)-5-phthalancarbonitrile oxalate.

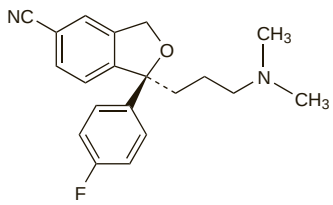
Эсциталопрама Оксалат

$C_{20}H_{21}FN_2O,C_2H_2O_4$ = 414.4.

CAS — 128196-01-0 (escitalopram); 219861-08-2 (escitalopram oxalate).

ATC — N06AB10.

ATC Vet — QN06AB10.



(escitalopram)

Adverse Effects and Precautions

As for Citalopram, p.385.

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.

Pharmacokinetics

Escitalopram has similar pharmacokinetics to those of racemic citalopram (p.385).

◊ References.

1. Søgaard B, *et al.* The pharmacokinetics of escitalopram after oral and intravenous administration of single and multiple doses to healthy subjects. *J Clin Pharmacol* 2005; **45:** 1400–6.
2. Rao N. The clinical pharmacokinetics of escitalopram. *Clin Pharmacokinet* 2007; **46:** 281–90.

Uses and Administration

Escitalopram, the *S*-enantiomer of citalopram (p.385), is an SSRI with actions and uses similar to those of fluoxetine (p.391). It is given orally as the oxalate although doses are expressed in terms of the base; escitalopram oxalate 12.8 mg is equivalent to about 10 mg of escitalopram.

In the treatment of **depression**, the usual dose is 10 mg once daily increased, after at least a week, to a maximum of 20 mg once daily if necessary.

Escitalopram is also used in the treatment of **panic disorder** with or without agoraphobia. Initial doses are 5 mg once daily, increased after a week to 10 mg once daily; further increases up to a maximum of 20 mg daily may be necessary in some patients.

Doses of escitalopram used in the treatment of **generalised anxiety disorder**, **social anxiety disorder**, and **obsessive-compulsive disorder** are similar to those used in depression.

Initial treatment with half the usual recommended dose and a lower maximum dose should be considered in elderly patients. Patients with hepatic impairment or those who are poor metabolisers with respect to the cytochrome P450 isoenzyme CYP2C19 may also require lower doses (see below).

Escitalopram should be withdrawn gradually to reduce the risk of withdrawal symptoms.

Administration in hepatic impairment. Increases of 51% and 69% in the area under the concentration-time curve occurred in a single-dose study of escitalopram in patients with mild and moderate hepatic impairment (Child-Pugh score 5 or 6, and 7 to 9, respectively).[1] This study also reported that activity of the cytochrome P450 isoenzyme CYP2C19 was a better predictor of escitalopram clearance than the Child-Pugh classification.

UK licensed product information for escitalopram suggests that patients with mild to moderate hepatic impairment or those who are poor metabolisers with respect to the cytochrome P450 isoenzyme CYP2C19 should receive an initial oral dose of 5 mg daily, increased to 10 mg daily after 2 weeks depending on response; more careful dose titration is advised in those with severe impairment. US licensed product information recommends 10 mg daily as a suitable dose for most patients with hepatic impairment.

1. Areberg J, *et al.* The pharmacokinetics of escitalopram in patients with hepatic impairment. *AAPS J* 2006; **8:** E14–E19.

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

References.

1. Stahl SM, *et al.* Escitalopram in the treatment of panic disorder: a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2003; **64:** 1322–7.
2. Davidson JR, *et al.* Escitalopram in the treatment of generalized anxiety disorder: double-blind, placebo controlled, flexible-dose study. *Depress Anxiety* 2004; **19:** 234–40.
3. Lader M, *et al.* Efficacy and tolerability of escitalopram in 12- and 24-week treatment of social anxiety disorder: randomised, double-blind, placebo-controlled, fixed-dose study. *Depress Anxiety* 2004; **19:** 241–8.
4. Kasper S, *et al.* Escitalopram in the treatment of social anxiety disorder: randomised, placebo-controlled, flexible-dosage study. *Br J Psychiatry* 2005; **186:** 222–6.
5. Stein DJ, *et al.* Escitalopram in obsessive-compulsive disorder: a randomized, placebo-controlled, paroxetine-referenced, fixed-dose, 24-week study. *Curr Med Res Opin* 2007; **23:** 701–11.

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

References.

1. Burke WJ, *et al.* Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. *J Clin Psychiatry* 2002; **63:** 331–6.
2. Wade A, *et al.* Escitalopram 10mg/day is effective and well tolerated in a placebo-controlled study in depression in primary care. *Int Clin Psychopharmacol* 2002; **17:** 95–102.
3. Lepola UM, *et al.* Escitalopram (10-20 mg/day) is effective and well tolerated in a placebo-controlled study in depression in primary care. *Int Clin Psychopharmacol* 2003; **18:** 211–17.
4. Rapaport MH, *et al.* Escitalopram continuation treatment prevents relapse of depressive episodes. *J Clin Psychiatry* 2004; **65:** 44–9.
5. Montgomery SA, *et al.* A randomised study comparing escitalopram with venlafaxine XR in primary care patients with major depressive disorder. *Neuropsychobiology* 2004; **50:** 57–64.
6. Murdoch D, Keam SJ. Escitalopram: a review of its use in the management of major depressive disorder. *Drugs* 2005; **65:** 2379–2404.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Aramix; Citalax; Lexapro; Lextor; Meridian; ***Austral.:*** Esipram; Lexapro; ***Austria:*** Cipralex; ***Belg.:*** Sipralexa; ***Braz.:*** Lexapro; ***Canad.:*** Cipralex; ***Chile:*** Celtium; Ectiban; Ipran; Lexapro; Neozentius; Zepaz; ***Cz.:*** Cipralex; ***Denm.:*** Cipralex; ***Fin.:*** Cipralex; ***Fr.:*** Seroplex; ***Ger.:*** Cipralex; ***Gr.:*** Cipralex; Entact; ***Hong Kong:*** Lexapro; ***Hung.:*** Cipralex; ***India:*** Cipralex; Recita; S-Citadep; ***Indon.:*** Cipralex; ***Irl.:*** Lexapro; ***Israel:*** Cipralex; ***Ital.:*** Cipralex; Entact; ***Malaysia:*** Lexapro; ***Mex.:*** Lexapro; ***Neth.:*** Cipralex; Lexapro; ***Norw.:*** Cipralex; ***NZ:*** Lexapro; ***Philipp.:*** Lexapro; ***Pol.:*** Lexapro; ***Port.:*** Cipralex; ***Rus.:*** Cipralex (Ципралекс); ***S.Afr.:*** Cipralex; ***Singapore:*** Lexapro; ***Spain:*** Cipralex; Entact; Esertia; ***Swed.:*** Cipralex; ***Switz.:*** Cipralex; ***Thai.:*** Lexapro; ***Turk.:*** Cipralex; ***UK:*** Cipralex; ***USA:*** Lexapro; ***Venez.:*** Lexapro.

Fluoxetine Hydrochloride

(BANM, USAN, rINNM)

Fluoksetiinihydrokloridi; Fluoksetin Hidroklorür; Fluoksetino hidrochloridas; Fluoksetyny chlorowodorek; Fluoxétine, chlorhydrate de; Fluoxetin-hidroklorid; Fluoxetin-hydrochlorid; Fluoxetinhydroklorid; Fluoxetini hydrochloridum; Hidrocloruro de fluoxetina; Lilly-103472; LY-110140. (±)-*N*-Methyl-3-phenyl-3-(α,α,α-trifluoro-*p*-tolyloxy)propylamine hydrochloride.

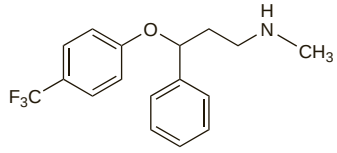
Флуоксетина Гидрохлорид

$C_{17}H_{18}F_3NO,HCl$ = 345.8.

CAS — 54910-89-3 (fluoxetine); 59333-67-4 (fluoxetine hydrochloride).

ATC — N06AB03.

ATC Vet — QN06AB03.



(fluoxetine)

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of fluoxetine:
Distas; Green and whites; Greens; Limes; Pros; Zacs.

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

Ph. Eur. 6.2 (Fluoxetine Hydrochloride). A white or almost white crystalline powder. Sparingly soluble in water and in dichloromethane; freely soluble in methyl alcohol. A 1% solution in water has a pH of 4.5 to 6.5.

USP 31 (Fluoxetine Hydrochloride). A white to off-white crystalline powder. Sparingly soluble in water and in dichloromethane; freely soluble in alcohol and in methyl alcohol; practically insoluble in ether. Store in airtight containers.

Adverse Effects

SSRIs such as fluoxetine are less sedating than tricyclic antidepressants and have fewer antimuscarinic and cardiotoxic effects. Adverse effects reported with SSRIs include dry mouth and gastrointestinal disturbances such as nausea, vomiting, dyspepsia, constipation, and diarrhoea. Anorexia and weight loss may also occur. Neurological adverse effects have included either anxiety, restlessness, nervousness, and insomnia, or drowsiness and fatigue; headache, tremor, dizziness, seizures, hallucinations, confusion, agitation, extrapyramidal effects, depersonalisation, mania, panic attacks, sexual dysfunction, and symptoms suggestive of a serotonin syndrome (p.416) have also occurred. The concern that SSRIs may be associated with increased suicidal ideation is discussed under Effects on Mental State, below.

Excessive sweating, pruritus, skin rashes, alopecia, photosensitivity, and urticaria have also been reported. Angioedema and anaphylactoid reactions have occurred. In some patients who have developed rashes while taking fluoxetine, systemic hypersensitivity reactions involving the lungs, kidneys, or liver, and possibly related to vasculitis, have developed; it has therefore been advised that fluoxetine therapy should be stopped in any patient who develops a skin rash.

Hyponatraemia, possibly due to inappropriate secretion of antidiuretic hormone, has been associated with the use of antidepressants, particularly in the elderly. Hyperprolactinaemia and galactorrhoea have occurred, as have changes in blood sugar, in patients receiving SSRIs.

Arthralgia and myalgia have been reported and there have also been cases of orthostatic hypotension, yawning, urinary retention, and abnormal vision including blurred vision and mydriasis. Abnormal liver function tests have been reported rarely. SSRIs have occasionally been associated with bleeding disorders such as ecchymosis and purpura and other effects on the blood.

In overdosage nausea, vomiting, and excitation of the CNS are considered to be prominent features; death has been reported.

Incidence of adverse effects. In June 1992 the UK CSM had received 1236 reports of adverse effects with fluvoxamine (from about 280 000 prescriptions) compared with 2422 for fluoxetine (from about 480 000 prescriptions).[1] The overall patterns of adverse effects were similar but dermatological reactions were more likely with fluoxetine and gastrointestinal reactions with fluvoxamine. Reports of attempted suicide increased after adverse publicity about SSRIs in 1990, and the number of reports per million prescriptions were similar for the 2 drugs (25 for fluoxetine and 20 for fluvoxamine); at that time such figures were not considered disconcerting given that features of depression, including attempted suicide, can worsen after the introduction of any antidepressant (see also Effects on Mental State, below). A later review[2] by the CSM of the 5 SSRIs available in the UK (citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) found that the SSRIs were broadly similar with respect to their safety profile. A list of adverse reactions common to all SSRIs was provided.

A review[3] of 1861 adverse reactions to citalopram, fluoxetine, fluvoxamine, paroxetine, or sertraline reported to the Swedish Adverse Drug Reactions Advisory Committee found that the most commonly reported reactions were neurological (22.4% of all reports), psychiatric (19.5%), and gastrointestinal (18.0%). Compared with other SSRIs, gastrointestinal symptoms were more common with fluvoxamine, psychiatric symptoms with sertraline, and dermatological symptoms with fluoxetine.

A more recent meta-analysis[4] has compared the adverse effect profile of fluoxetine with other antidepressants including the tricyclics and other SSRIs. The overall risk of any adverse effect with fluoxetine was less than that for the tricyclic antidepressants; however, there was no difference in risk when fluoxetine was compared with other SSRIs. When considering individual adverse reactions, fluoxetine was more likely to cause activating