Sertraline should be used with caution in patients with hepatic or renal impairment; reduced doses should be considered in patients with hepatic impairment.

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

Sertraline is slowly absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 4.5 to 8.4 hours after ingestion. It undergoes extensive first-pass metabolism in the liver. The main pathway is demethylation to inactive *N*-desmethylsertraline, a process that appears to involve multiple cytochrome P450 isoenzymes; further metabolism and glucuronide conjugation occurs. Sertraline is widely distributed throughout body tissues and is about 98% bound to plasma proteins. The plasma elimination half-life of sertraline is reported to be about 26 hours; steady-state concentrations are achieved after about one week with regular oral doses. Sertraline is excreted in about equal amounts in the urine and faeces, mainly as metabolites. Sertraline is distributed into breast milk (see Breast Feeding under Precautions in Fluoxetine, p.394).

◊ References.

1. Preskorn SH, ed. Sertraline: a pharmacokinetic profile. *Clin Pharmacokinet* 1997; **32** (suppl 1): 1–55.
2. Hiemke C, Härtter S. Pharmacokinetics of selective serotonin reuptake inhibitors. *Pharmacol Ther* 2000; **85:** 11–28.
3. Wang J-H, *et al.* Pharmacokinetics of sertraline in relation to genetic polymorphism of CYP2C19. *Clin Pharmacol Ther* 2001; **70:** 42–7.
4. DeVane CL, *et al.* Clinical pharmacokinetics of sertraline. *Clin Pharmacokinet* 2002; **41:** 1247–66.
5. Obach RS, *et al.* Sertraline is metabolized by multiple cytochrome P450 enzymes, monoamine oxidases, and glucuronyl transferases in human: an in vitro study. *Drug Metab Dispos* 2005; **33:** 262–70.

Uses and Administration

Sertraline, a naphthaleneamine derivative, is an SSRI with actions and uses similar to those of fluoxetine (p.397). It is given orally as sertraline hydrochloride as a single dose in the morning or evening. Doses are expressed in terms of the base; sertraline hydrochloride 56 mg is equivalent to about 50 mg of sertraline.

In the treatment of **depression**, the usual initial dose of sertraline is 50 mg daily increased, if necessary, in increments of 50 mg at intervals of at least a week to a maximum of 200 mg daily.

The usual initial dose of sertraline in **obsessive-compulsive disorder** is 50 mg daily. In the treatment of **panic disorder** with or without agoraphobia, **social anxiety disorder**, and **post-traumatic stress disorder**, the usual initial dose is 25 mg daily increased after one week to 50 mg daily. Thereafter, doses in all these disorders may be increased, if necessary, in increments of 50 mg at intervals of at least a week to a maximum of 200 mg daily.

Sertraline is also given for the treatment of obsessive-compulsive disorder in *children and adolescents* aged 6 years and over. In children aged 6 to 12 years the usual initial dose is 25 mg once daily; adolescents may be started on 50 mg once daily. Increases in doses, if necessary, are similar to those in adults; however, the lower body-weights of children should be considered in order to avoid excessive doses.

In the treatment of **premenstrual dysphoric disorder**, sertraline is given in an initial dose of 50 mg daily either throughout the menstrual cycle or during the luteal phase only, as appropriate. Doses may be increased by 50 mg each menstrual cycle up to a maximum of 150 mg daily for continuous dosing or 100 mg daily when dosing during the luteal phase only. Those patients who require 100 mg daily during luteal phase-only dosing should initially be given 50 mg daily for the first 3 days of each luteal phase dosing period.

Once the optimal therapeutic response is obtained dosage should be reduced to the lowest effective level for maintenance.

Reduced doses are recommended in patients with hepatic impairment, see below.

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

Administration in hepatic impairment. The clearance of sertraline was reduced in patients with liver cirrhosis, in a single-dose pharmacokinetic study.[1] US licensed product information states that in a small group of patients with chronic mild impairment (Child-Pugh scores of 5 to 8), given 50 mg daily for 21 days, exposure to sertraline was about 3 times that found in subjects with normal hepatic function. It also states that the effects of sertraline have not been studied in moderate and severe impairment. If sertraline is to be used in patients with hepatic impairment, it suggests that the drug should be used with caution and given at a lower dose or less frequently. UK product information considers sertraline to be contra-indicated in significant hepatic impairment, because of insufficient clinical experience.

1. Démolis J-L, *et al.* Influence of liver cirrhosis on sertraline pharmacokinetics. *Br J Clin Pharmacol* 1996; **42:** 394–7.

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

References.

1. March JS, *et al.* Sertraline in children and adolescents with obsessive-compulsive disorder: a multicenter randomized controlled trial. *JAMA* 1998; **280:** 1752–6.
2. Londborg PD, *et al.* Sertraline in the treatment of panic disorder. A multi-site, double-blind, placebo-controlled, fixed-dose investigation. *Br J Psychiatry* 1998; **173:** 54–60.
3. Brady K, *et al.* Efficacy and safety of sertraline treatment of posttraumatic stress disorder: a randomized controlled trial. *JAMA* 2000; **283:** 1837–44.
4. Walker JR, *et al.* Prevention of relapse in generalized social phobia: results of a 24-week study in responders to 20 weeks of sertraline treatment. *J Clin Psychopharmacol* 2000; **20:** 636–44.
5. Rynn MA, *et al.* Placebo-controlled trial of sertraline in the treatment of children with generalized anxiety disorder. *Am J Psychiatry* 2001; **158:** 2008–14.
6. Rapaport MH, *et al.* Sertraline treatment of panic disorder: results of a long-term study. *Acta Psychiatr Scand* 2001; **104:** 289–98.
7. Rapaport MH, *et al.* Posttraumatic stress disorder and quality of life: results across 64 weeks of sertraline treatment. *J Clin Psychiatry* 2002; **63:** 59–65.
8. Koran LM, *et al.* Efficacy of sertraline in the long-term treatment of obsessive-compulsive disorder. *Am J Psychiatry* 2002; **159:** 88–95.
9. Zohar J, *et al.* Double-blind placebo-controlled pilot study of sertraline in military veterans with posttraumatic stress disorder. *J Clin Psychopharmacol* 2002; **22:** 190–5.
10. Liebowitz MR, *et al.* Efficacy of sertraline in severe generalized social anxiety disorder: results of a double-blind, placebo-controlled study. *J Clin Psychiatry* 2003; **64:** 785–92.
11. Allgulander C, *et al.* Efficacy of sertraline in a 12-week trial for generalized anxiety disorder. *Am J Psychiatry* 2004; **161:** 1642–9.

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. SSRIs such as sertraline are widely used as an alternative to the older tricyclics as they have fewer adverse effects and are safer in overdosage.

References.

1. Stowe ZN, *et al.* Sertraline in the treatment of women with postpartum major depression. *Depression* 1995; **3:** 49–55.
2. Keller MB, *et al.* Maintenance phase efficacy of sertraline for chronic depression: a randomized controlled trial. *JAMA* 1998; **280:** 1665–72.
3. Baca E, *et al.* Sertraline is more effective than imipramine in the treatment of non-melancholic depression: results from a multicentre, randomized study. *Prog Neuropsychopharmacol Biol Psychiatry* 2003; **27:** 493–500.
4. Lepine JP, *et al.* A randomized, placebo-controlled trial of sertraline for prophylactic treatment of highly recurrent major depressive disorder. *Am J Psychiatry* 2004; **161:** 836–42.
5. Moscovitch A, *et al.* A placebo-controlled study of sertraline in the treatment of outpatients with seasonal affective disorder. *Psychopharmacology (Berl)* 2004; **171:** 390–7.

Headache. For reference to the use of SSRIs, including sertraline, in the management of various types of headache, see under Fluoxetine, p.398.

Premenstrual syndrome. Sertraline throughout the menstrual cycle has produced beneficial effects in controlling both the psychological and somatic symptoms of women with premenstrual syndrome (p.2099).[1-3] Giving sertraline solely during the luteal phase was also of benefit.[3-6]

1. Yonkers KA, *et al.* Sertraline in the treatment of premenstrual dysphoric disorder. *Psychopharmacol Bull* 1996; **32:** 41–6.
2. Yonkers KA, *et al.* Symptomatic improvement of premenstrual dysphoric disorder with sertraline treatment: a randomized controlled trial. *JAMA* 1997; **278:** 983–8.
3. Freeman EW, *et al.* Continuous or intermittent dosing with sertraline for patients with severe premenstrual syndrome or premenstrual dysphoric disorder. *Am J Psychiatry* 2004; **161:** 343–51.
4. Young SA, *et al.* Treatment of premenstrual dysphoric disorder with sertraline during the luteal phase: a randomized, double-blind, placebo-controlled crossover trial. *J Clin Psychiatry* 1998; **59:** 76–80.
5. Jermain DM, *et al.* Luteal phase sertraline treatment for premenstrual dysphoric disorder: results of a double-blind, placebo-controlled, crossover study. *Arch Fam Med* 1999; **8:** 328–32.
6. Halbreich U, *et al.* Efficacy of intermittent, luteal phase sertraline treatment of premenstrual dysphoric disorder. *Obstet Gynecol* 2002; **100:** 1219–29.

Sexual dysfunction. Impotence or ejaculatory problems have been reported as adverse effects of SSRIs; for the use of these effects as a potential form of management for premature ejaculation see Fluoxetine, p.399.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Anilar; Atenix; Bicromil; Celonfex; Deprecalm; Insertec; Irradial; Serlina; Servantax; Vunot; Zoloft; ***Austral.:*** Eleva; Setrona; Xydep; Zoloft; ***Austria:*** Gladem; Sertrex; Tresleen; ***Belg.:*** Serlain; ***Braz.:*** Assert; Novativ; Sercerin†; Serenata; Seronip†; Tolrest; Zoloft; ***Canad.:*** Zoloft; ***Chile:*** Altruline; Deprax; Eleval; Emergen; Implicane; Lowfin; Sedoran; Serivo; Seronex; Sertac; Tralinser; ***Cz.:*** Adjuvin; Apo-Sertral; Asentra; Serlift; Setaloft; Stimuloton; Zoloft; ***Denm.:*** Zoloft; ***Fin.:*** Zoloft; ***Fr.:*** Zoloft; ***Ger.:*** Gladem; Sertra; Zoloft; ***Gr.:*** Certorun; Enidap; Neurosedine; Zoloft; Zolotrin; ***Hong Kong:*** Stimuloton; Zoloft; ***Hung.:*** Asentra; Gerotralin; Serlift; Serlosane; Sertadepi; Sertagen; Sertwin; Stimuloton; Zoloft; ***India:*** Inosert; Serdep; Serta; Xsert; ***Indon.:*** Antipres; Deptral; Fatral; Fridep; Nudep; Serlof; Sernade; Zerlin; Zoloft; ***Irl.:*** Depreger; Lusert; Lustral; Serimel; Serlan; Sertraniche; ***Israel:*** Lustral; ***Ital.:*** Tatig; Zoloft; ***Malaysia:*** Serlift; Zoloft; ***Mex.:*** Aleval; Altruline; Aluprex; Deptral; Prosertin; Serolux; Sertex; ***Neth.:*** Asentra; Zoloft; ***Norw.:*** Zoloft; ***NZ:*** Zoloft; ***Philipp.:*** Serenata; Zoloft; ***Pol.:*** Asentra; Luxeta; Sertahexal; Setaloft; Setaratio; Stimuloton; Zoloft; Zotral; ***Port.:*** Zoloft; ***Rus.:*** Asentra (Асентра); Serenata (Серената); Stimuloton (Стимулотон); Torin (Торин); Zoloft (Золофт); ***S.Afr.:*** Serdep; Serlife; Sertzol; Zoloft; ***Singapore:*** Zoloft; ***Spain:*** Altisben; Aremis; Besitran; Depesert; Sealdin†; ***Swed.:*** Zoloft; ***Switz.:*** Gladem; Zoloft; ***Thai.:*** Zoloft; ***Turk.:*** Lustral; Selectra; Seralin; Serdep; ***UK:*** Lustral; ***USA:*** Zoloft; ***Venez.:*** Conexine; Lusedan; Satil; Serline; Serolux; Tialin; Zoloft.

Multi-ingredient: ***India:*** Restyl Forte; Restyl Plus.

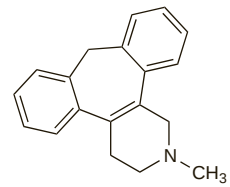
Setiptiline *(rINN)*

Setiptilina; Sétiptiline; Setiptilinum; Teciptiline. 2,3,4,9-Tetrahydro-2-methyl-1*H*-dibenzo[3,4:6,7]cyclohepta[1,2-*c*]pyridine.

Сетиптилин

$C_{19}H_{19}N$ = 261.4.

CAS — 57262-94-9 (setiptiline); 85650-57-3 (setiptiline maleate).



Profile

Setiptiline is an antidepressant that has been used as the maleate in the treatment of depression.

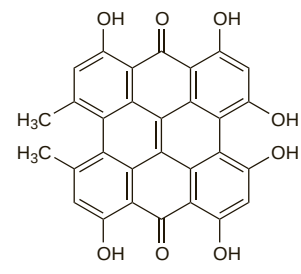
Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Tecipul.

St John's Wort

Hipérico; Hiperikum; Hyperici herba; Hypericum; Johannesört; Johanniskraut; Jonažolių žolė; Mäkikuisma; Millepertuis; Orbáncfű; Třezalková nať; Ziele dziurawca.

CAS — 548-04-9 (hypericin).



(hypericin)

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Eur. also includes a form for homoeopathic preparations.
Swiss also includes monographs for hypericum (fresh flowering tops) and hypericum oil.
Ph. Eur. 6.2 (St John's Wort). The whole or cut, dried flowering tops of *Hypericum perforatum* gathered during flowering. It con-