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.

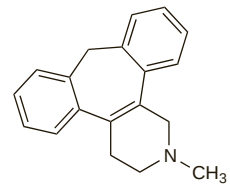
Setiptiline *(rINN)*

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.

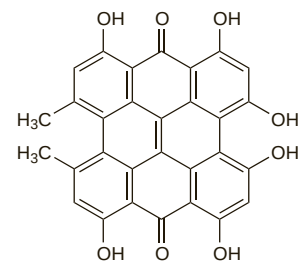
Preparations

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-

tains not less than 0.08% of total hypericins, expressed as hypericin ($C_{30}H_{16}O_8$ = 504.4) calculated with reference to the dried drug. Protect from light.

Ph. Eur. 6.2 (Hypericum for Homoeopathic Preparations; Hypericum Perforatum ad Praeparationes Homoeopathicas). The whole, fresh plant of *Hypericum perforatum*, at the beginning of the flowering period. Protect from light.

USP 31 (St. John's Wort). The dried flowering tops or aerial parts of *Hypericum perforatum* (Hypericaceae), gathered shortly before or during flowering. It contains not less than 0.04% of the combined total of hypericin ($C_{30}H_{16}O_8$ = 504.4) and pseudohypericin ($C_{30}H_{16}O_9$ = 520.4) and not less than 0.6% of hyperforin ($C_{35}H_{52}O_4$ = 536.8). Store in airtight containers. Protect from light.

Adverse Effects and Precautions

Adverse effects reported with St John's wort have included gastrointestinal symptoms, dizziness, headache, confusion, urinary frequency, allergic reactions, and fatigue. Photosensitivity has also been reported; hypericin and pseudohypericin are the constituents of St John's wort thought to be responsible for this reaction.

Effects on the nervous system. Subacute polyneuropathy after sun exposure developed in a woman who had taken St John's wort for mild depression; she improved after drug withdrawal.[1] Seizures and confusion occurred in a 16-year-old girl after an overdose of St John's wort.[2] She had taken large daily doses for 2 weeks and an overdose just before presentation.

1. Bove GM. Acute neuropathy after exposure to sun in a patient treated with St John's Wort. *Lancet* 1998; **352:** 1121–2.
2. Karalapillai DC, Bellomo R. Convulsions associated with an overdose of St John's wort. *Med J Aust* 2007; **186:** 213–14.

Effects on the skin. In addition to photosensitivity reactions associated with St John's wort use,[1] there has been a report of severe erythroderma in a patient who supplemented his regular antidepressant medication (dosulepin) with St John's wort.[2] The reaction was seen on both light-exposed and non-exposed areas, and was thought to be due to the St John's wort although there remained a possibility that it was due to an interaction between the 2 drugs.

1. Lane-Brown MM. Photosensitivity associated with herbal preparations of St John's wort (Hypericum perforatum). *Med J Aust* 2000; **172:** 302.
2. Holme SA, Roberts DL. Erythroderma associated with St John's wort. *Br J Dermatol* 2000; **143:** 1127–8.

Mania. There have been a number of cases of mania or hypomania associated with the use of St John's wort.[1-3]

1. Neirenberg AA, *et al.* Mania associated with St John's wort. *Biol Psychiatry* 1999; **46:** 1707–8.
2. Fahmi M, *et al.* A case of mania induced by hypericum. *World J Biol Psychiatry* 2002; **3:** 58–9.
3. Stevinson C, Ernst E. Can St John's wort trigger psychoses? *Int J Clin Pharmacol Ther* 2004; **42:** 473–80.

Withdrawal. A 58-year-old woman developed symptoms such as nausea, anorexia, dizziness, dry mouth, thirst, chills, and fatigue the day after stopping St John's wort;[1] she had taken the drug for 32 days. The symptoms, which the authors considered suggestive of a withdrawal syndrome, resolved within 8 days.

1. Dean AJ, *et al.* Suspected withdrawal syndrome after cessation of St John's wort. *Ann Pharmacother* 2003; **37:** 150.

Interactions

St John's wort has been shown to induce several drug metabolising enzymes including some cytochrome P450 isoenzymes (in particular CYP3A4) and the transport protein P-glycoprotein. Clinically important interactions resulting in decreased plasma concentrations of the interacting drug have been reported with ciclosporin, digoxin, HIV-protease inhibitors, NNRTIs, oral contraceptives, tacrolimus, theophylline, and warfarin. There is also a possibility of an interaction between St John's wort and antiepileptics. In addition, stopping St John's wort may result in increased, and possibly toxic, concentrations of the interacting drug.

In many countries, including the UK and USA, preparations of St John's wort are not required to be licensed as medicines, and the amount of active ingredient may vary widely between preparations. Changing preparations may therefore alter the degree of enzyme induction.

Use of St John's wort with drugs known to act on serotonergic neurotransmitters may result in synergistic interactions and an increased risk of adverse effects may also occur. Examples include the SSRIs and nefazodone (see Antidepressants, p.418) and the selective serotonin (5-HT_1) agonists (see under Sumatriptan, p.626) used to treat migraine.

◊ References.

1. Roby CA, *et al.* St John's Wort: effect on CYP3A4 activity. *Clin Pharmacol Ther* 2000; **67:** 451–7.
2. CSM/MCA. Reminder: St John's Wort (Hypericum perforatum) interactions. *Current Problems* 2000; **26:** 6–7. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007462&RevisionSelectionMethod=LatestReleased (accessed 24/11/05)
3. Dürr D, *et al.* St John's Wort induces intestinal p-glycoprotein/MDR1 and intestinal and hepatic CYP3A4. *Clin Pharmacol Ther* 2000; **68:** 598–604.
4. Wang Z, *et al.* The effects of St John's wort (*Hypericum perforatum*) on human cytochrome P450 activity. *Clin Pharmacol Ther* 2001: **70:** 317–26.
5. Hennessy M, *et al.* St John's Wort increases expression of P-glycoprotein: implications for drug interactions. *Br J Clin Pharmacol* 2002 **53:** 75–82.
6. Henderson L, *et al.* St John's wort (*Hypericum perforatum*): drug interactions and clinical outcomes. *Br J Clin Pharmacol* 2002; **54:** 349–56.
7. Mills E, *et al.* Interaction of St John's wort with conventional drugs: systematic review of clinical trials. *BMJ* 2004; **329:** 27–30.
8. Mannel M. Drug interactions with St John's wort: mechanisms and clinical implications. *Drug Safety* 2004; **27:** 773–97.
9. Whitten DL, *et al.* The effect of St John's wort extracts on CYP3A: a systematic review of prospective clinical trials. *Br J Clin Pharmacol* 2006; **62:** 512–26.

Analgesics. For details of a possible interaction between St John's wort and the opioid analgesic *methadone*, see p.84.

Anticoagulants. For mention of a possible interaction between St John's wort and *warfarin*, see p.1432.

Antiepileptics. There is a possibility of an interaction between St John's wort and antiepileptics such as *carbamazepine* (see p.474), *phenobarbital* (see p.493), and *phenytoin* (see p.498).

Antineoplastics. St John's wort may interact with some antineoplastics; examples include *aminolevulinic acid* (see p.679), *imatinib* (see p.734), and *irinotecan* (see p.737).

Antivirals. For details of a possible interaction between St John's wort and *HIV-protease inhibitors* such as indinavir, see p.883.

Cardiac glycosides. For details of a possible interaction between St John's wort and *digoxin*, see p.1261.

Immunosuppressants. For details of possible interactions between St John's wort and *ciclosporin* or *tacrolimus*, see p.1826 and p.1845, respectively.

Oral contraceptives. For reports of a possible interaction between St John's wort and oral contraceptives, see p.2068.

Verapamil. For details of a possible interaction between St John's wort and verapamil, see p.1423.

Xanthines. For details of a possible interaction between St John's wort and *theophylline*, see p.1143.

Uses and Administration

Herbal preparations containing St John's wort are used, frequently for self-medication, in the treatment of depression. Such preparations are also promoted for the treatment of other nervous disorders such as insomnia and anxiety, particularly if associated with the menopause. St John's wort oil has also been used as an astringent. Hypericin, a major constituent of St John's wort, has been investigated as an antiviral in the treatment of HIV infection and AIDS (but see Antiviral Action, below).

The amount of active constituents can vary between different preparations and doses depend on the preparation being used.

Homoeopathy. St John's wort has been used in homoeopathic medicines under the following names: Hypericum; Hypericum perforatum; Hypericum perforatum ex herba; Hypericum, herba; Hyper.

◊ References.

1. McIntyre M. A review of the benefits, adverse events, drug interactions, and safety of St John's Wort (Hypericum perforatum): the implications with regard to the regulation of herbal medicines. *J Altern Complement Med* 2000; **6:** 115–24.

Antiviral action. A study involving 30 HIV-infected patients suggested that hypericin, given intravenously or by mouth, produced significant phototoxicity and had no effect on virological markers or CD4 cell count.[1]

1. Gulick RM, *et al.* Phase I studies of hypericin, the active compound in St John's Wort, as an antiretroviral agent in HIV-infected adults. *Ann Intern Med* 1999; **130:** 510–14.

Depression. St John's wort extracts are widely used in some countries for the treatment of depression (p.373).

Two systematic reviews[1,2] of randomised controlled studies found St John's wort extracts to be more effective than placebo in the treatment of mild to moderate depressive disorders. However, the results of the more recent review[2] also suggested that St John's wort extracts were only of minor benefit in patients with major depression and probably of no benefit in those with a prolonged history of the condition; in addition, there was no evidence of effectiveness in severe depression. The authors of this review commented that recent placebo-controlled studies tended to show less favourable results for St John's wort than older studies. It was considered that the heterogeneous findings were due partly to overestimation of effects in some smaller, older studies, and partly to the variable efficacy of St John's wort extracts in different patient populations; non-publication of negative studies was not thought to have played a major role.

The efficacy of St John's wort compared with standard antidepressants has also been reviewed and found to be comparable.[2] However, this finding should be interpreted with caution, not least because doses of the standard antidepressants used were at the lower end of the range in some studies.

The mechanism of action of St John's wort extracts in the treatment of depression remains unclear. Extracts contain at least 10 active principles. Hypericin, one of the major constituents of St John's wort, was first thought responsible for the antidepressant effect since it had an inhibitory action on monoamine oxidase *in vitro*. However it was later shown that this action was, at best, weak and it is now generally believed that monoamine oxidase inhibition is not responsible for the antidepressant effect of St John's wort. More recent studies have suggested that hyperforin may be one of the major constituents responsible for the antidepressant effect.[3] Although the evidence is mainly from *in vitro* studies, hyperforin inhibits the reuptake of several major neurotransmitters including serotonin, dopamine, and noradrenaline.[4]

1. Stevinson C, Ernst E. Hypericum for depression: an update of the clinical evidence. *Eur Neuropsychopharmacol* 1999; **9:** 501–5.
2. Linde K, *et al.* St John's wort for depression. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2005 (accessed 24/11/05).
3. Laakmann G, *et al.* St. John's Wort in mild to moderate depression: the relevance of hyperforin for the clinical efficacy. *Pharmacopsychiatry* 1998: **31** (suppl.): 54–9.
4. Chatterjee SS, *et al.* Hyperforin as a possible antidepressant component of hypericum extracts. *Life Sci* 1998; **63:** 499–510.

Preparations

Ph. Eur.: St John's Wort Dry Extract, Quantified.

Proprietary Preparations (details are given in Part 3)
Arg.: Amenicil; Felis†; Herbaccion Motivante†; Hipax; Hiperinat; Remotiv†; ***Austral.:*** Bioglan Stress-Relax; Hyperiforte†; Remotiv; ***Austria:*** Esbericum; Felis†; Helarium; Hyperiforce; Jarsin; Johanicum; Johni; Kira; Lunare; Perikan; Psychotonin; Remotiv; Solaguttae; ***Belg.:*** Hyperiplant; Milperinol; Perika; ***Braz.:*** Adprex†; Ciperico; Emotival†; Equilibra†; Fiotan; Fitovital; Hiperex; Hipericin; Hiperico; Hiperifarma†; Hiperil†; Hipersac; Hyperico†; Hyperigreen; Iperisan; Jarsin†; Motiven; Prazen; Remotiv; Triativ; ***Canad.:*** Kira; Movana†; ***Chile:*** Anxium; Ciplazin†; Edual†; Remotiv†; ***Cz.:*** Cesradyston†; Deprim†; Esbericum†; Felisio; Helarium; Hyperikan; Jarsin; Kira†; Laif; Lubovnik†; Nat Trezalky; Psychotonin Forte†; Remotiv; Trezalka v Nalevovych Sacchich; Trezalkova Nat; Trezalkovy Caj; Turineurin†; ***Fr.:*** Bains Romains; Dermum†; Mildac; Procalmil; ***Ger.:*** aar brain N†; Aristo; Aristoforat; Cesradyston; dysto-lux; Esbericum; Felis; Helarium; Herbaneurin†; Hewepsychon uno; Hyperforat; Hypericaps†; Hyperimerck; Hyperpur; Jarsin; Jo-Sabona†; Kira; Kytta-Modal†; Laif; Libertin†; Lomahypericum†; Nervei; Neuroplant; Neurosporal; Neurovegetalin; Psychotonin; Psychotonin M†; Remotiv; Sedovegan†; Syxal†; Texx; Tonizin; Turineurin; Viviplus†; ***Gr.:*** Neukan; ***Hung.:*** Helarium; Hyperikan; Klosterfrau Sedinal; Myrall; Remotiv; ***Indon.:*** Preso; ***Israel:*** Remotiv; ***Ital.:*** Nervaxon; Proserem; Quiens; Remotive; ***Mex.:*** Hiperikan; Nutegen H†; Procalm†; Remotiv; ***Pol.:*** Apatinac; Deprim; Hyperherba; Hyperosedat; Perhip; Remotiv; Silenil; ***Port.:*** Alacre; ***Rus.:*** Deprim (Деприм); Doppelherz Nervotonik (Доппельгерц Нервотоник); Helarium (Гелариум); Negrustin (Негрустин); Novo-Passit (Ново-Пассит); ***S.Afr.:*** Remotiv†; ***Spain:*** Animic; Arkocapsulas Hiperico; Hiperico; Hyneurin; Perika; Quetzal; Vitalium; ***Switz.:*** Hyperforat†; Hypericettes†; Hyperiforce; HyperiMed; Hyperiplant; Hyperval; Jarsin; Libertin†; Lucilium; ReBalance; Remotiv; Solevita; Yakona; ***Turk.:*** Felis; ***UK:*** Hyperi-Calm; Kira; ***Venez.:*** Hyperikan; Kira†; Qual†.

Multi-ingredient: ***Austral.:*** Bioglan 3B Beer Belly Buster; Cimicifuga Compound; Feminine Herbal Complex; Infant Tonic†; Joint & Muscle Cream; Nappy Rash Relief Cream; Nevaton; Skin Healing Cream†; ***Austria:*** Eryval; Magentee St Severin; Nerventee St Severin; Remifemin plus; Species nervinae; Vulpuran; Wechseltee St Severin; ***Cz.:*** Alvisan Neo; Cajova Smes pri Redukcni Diete†; Cicaderma; Eugastrin†; Fytokliman Planta; Naturidentt; Novo-Passit; Species Nervinae Planta; Stomaran; Zaludecni Cajova Smes; ***Fr.:*** Cicaderma; ***Ger.:*** Allya†; anabol-loges; Anisan†; Arthrodynat P†; Befelka-Oel; Cheirantho†; Dolo-cyl; Gastritol; Gastrol S†; Gutnacht†; Hewepsychon duo†; Hyperesa; Hyperforat-forte†; JuDorm†; JuViton†; Marianon†; Me-Sabona plus†; Neurapas; Oxacant N†; Phytogran†; Presselin Arterien K 5 P†; Presselin Nerven K 1 N†; Psychotonin-sed; Remifemin plus; Rhoival†; Sedariston Konzentrat; Sedariston plus; Venacton†; ***Hung.:*** Remifemin Plus; ***Ital.:*** Controller; Hiperogyn; Mithen; Skab 2; ***Malaysia:*** Gyno-Plus; ***Mex.:*** Nordimenty; ***Pol.:*** Cholesol; Diges-Tonic; Fortestomachicae; Gastrobonisol; Guttae Stomachicae; Herbogastrin; Krople Zoladkowe; Melisal; Melissed; Nervomix; Perfocrat; Prostapol; Psychotonisol; Sedomix; Uroprost; ***Port.:*** Cicaderma; ***Rus.:*** Prostanorm (Простанорм); Sibectan (Сибектан); ***Spain:*** Natusor Gastrolen†; Natusor Somnisedan†; ***Switz.:*** Gel a la consoude; Huile de millepertuis A. Vogel (huile de St. Jean); Hyperiforce comp; Keppur; Kytta Gel†; Malvedrin; Saltrates Rodell†; Saltrates†; The a l'avoine sauvage de Vollmer; Yakona N†; Ziegella; ***UK:*** St Johnswort Compound; Tranquil; ***Venez.:*** Biomicovo†.

Tianeptine Sodium *(rINNM)*

Natrii Tianeptinum; Taneptinum Natricum; Tianeptiininatrium; Tianeptin sodná sůl; Tianeptin Sodyum; Tianeptina sódica; Tianeptine sodique; Tianeptinnatrium; Tianeptin-nátrium; Tianeptino natrio druska; Tianeptinum natricum. The sodium salt of 7-[(3-chloro-6,11-dihydro-6-methyldibenzo[*c*,*f*][1,2]thiazepin-11-yl)amino]heptanoic acid *S*,*S*-dioxide.

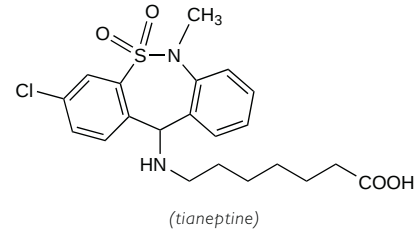
Натрий Тианептин

$C_{21}H_{24}ClN_2NaO_4S$ = 458.9.

CAS — 66981-73-5 (tianeptine).

ATC — N06AX14.

ATC Vet — QN06AX14.



(tianeptine)

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

Ph. Eur. 6.2 (Tianeptine Sodium). A white or yellowish, very hygroscopic, powder. Freely soluble in water, in dichloromethane, and in methyl alcohol. Store in airtight containers.