SISALON 50

ANTIDEPRESSANT

Each film coated tablet contains:
Sertraline hydrochloride eq. to
Sertraline 50 mg

✧ PRODUCT DESCRIPTION:

White, oblong, biconvex, film coated tablet with engraved S L on one side and 50 on the other scored side

✧ MECHANISM OF ACTION:

Pharmacology

Sertraline is a potent and specific inhibitor of neuronal serotonin (5 HT) uptake *in vitro*, which results in the potentiation of the effects of 5-HT in animals. It has only very weak effects on norepinephrine and dopamine neuronal reuptake. At clinical doses, Sertraline blocks the uptake of serotonin into human platelets. It is devoid of stimulant, sedative or anticholinergic activity or cardiotoxicity in animals.

Pharmacokinetics

Absorption

Sertraline exhibits dose proportional pharmacokinetics in the range of 50 to 200 mg. In man, following an oral once-daily dosage of 50 to 200 mg for 14 days, peak plasma concentrations of Sertraline occur at 4.5 to 8.4 hours after the daily administration of the drug. Food does not significantly change the bioavailability of Sertraline tablets.

Distribution

Approximately 98% of the circulating drug is bound to plasma proteins.

Biotransformation

Sertraline undergoes extensive first-pass hepatic metabolism.

Elimination

The mean half-life of Sertraline is approximately 26 hours (range 22-36 hours). Consistent with the terminal elimination half-life, there is an approximately two-fold accumulation up to steady state concentrations, which are achieved after one week of once-daily dosing. The half-life of N-desmethylsertraline is in the range of 62 to 104 hours. Sertraline and N-desmethylsertraline are both extensively metabolized in man and the resultant metabolites excreted in feces and urine in equal amounts. Only a small amount (< 0.2%) of unchanged Sertraline is excreted in the urine.

Pharmacokinetics in specific patient groups

Adolescents and elderly

The pharmacokinetic profile in adolescents or elderly is not significantly different from that in adults between 18 and 65 years.

Liver function impairment

In patients with liver damage, the half life of Sertraline is prolonged and AUC is increased three fold.

Renal impairment

In patients with moderate-severe renal impairment, there was no significant accumulation of Sertraline.

Pharmacogenomics

Plasma levels of Sertraline were about 50% higher in poor metabolizers of CYP2C19 versus extensive metabolizers. The clinical meaning is not clear, and patients need to be titrated based on clinical response.

✧ INDICATION#:

Sertraline is indicated for the treatment of symptoms of depression, including depression accompanied by symptoms of anxiety, in patients with or without a history of mania. Following satisfactory response, continuation with Sertraline therapy is effective in preventing relapse of the initial episode of depression or recurrence of further depressive episodes.
Sertraline is indicated for the treatment of obsessive-compulsive disorder (OCD). Following satisfactory response, continuation with Sertraline therapy is effective in preventing relapse of the initial episode of OCD.
Sertraline is indicated for the treatment of panic disorder, with or without agoraphobia. Following satisfactory response, continuation with Sertraline therapy is effective in preventing relapse of the initial episode of panic disorder.
Sertraline is indicated for the treatment of post-traumatic stress disorder (PTSD).

Following satisfactory response, continuation with Sertraline therapy is effective in preventing relapse of the initial episode of PTSD.
Sertraline is indicated for the treatment of social phobia (social anxiety disorder). Following satisfactory response, continuation with Sertraline therapy is effective in preventing relapse of the initial episode of social phobia.

✧ DOSAGE AND ADMINISTRATION#:

Oral
Sertraline should be administered once daily either in the morning or evening. Sertraline tablets can be administered with or without food.

Initial treatment

Depression and OCD

Sertraline treatment should be administered at a dose of 50 mg/day.

Panic Disorder, PTSD and Social Phobia

Therapy should be initiated at 25 mg/day. After one week the dose should be increased to 50 mg once daily. This dosage regimen has been shown to reduce the frequency of early treatment emergent side effects characteristic of panic disorder.

Titration

Depression, OCD, Panic Disorder, Social Anxiety Disorder and PTSD

Patients not responding to a 50 mg dose may benefit from dose increases. Dose changes should be made at interval of at least one week, up to a maximum of 200 mg/day. Changes in dose should not be made more frequently than once per week given the 24 hour elimination half life of Sertraline.
The onset of therapeutic effect may be seen within 7 days. However, longer periods are usually necessary to demonstrate therapeutic response especially in OCD.

Maintenance

Dosage during long-term therapy should be kept at the lowest effective level with subsequent adjustment depending on therapeutic response.

Use in children

The safety and effectiveness of Sertraline in children have not been fully established. In patients aged 6-17 with depression or OCD, Sertraline appeared to have a similar pharmacokinetic profile to that found in adults.

Use in the elderly

The same dose range as in younger patients may be used in the elderly. The pattern and incidence of adverse reactions in the elderly (>65 years) has been reported to be similar to that in younger patients.

Use in hepatic insufficiency

The use of Sertraline in patients with hepatic disease should be approached with caution. A lower or less frequent dose should be used in patients with hepatic impairment.

Use in renal insufficiency

Sertraline is extensively metabolized. Excretion of unchanged drug, in urine is a minor route of elimination. As expected from the low renal excretion of Sertraline, Sertraline dosing does not have to be adjusted based on the degree of renal impairment.

✧ WARNING AND PRECAUTION#:

Serotonin Syndrome (SS) or Neuroleptic Malignant Syndrome (NMS)

The development of potentially life-threatening syndromes like serotonin syndrome (SS) or Neuroleptic Malignant Syndrome (NMS) has been reported with SSRIs, including treatment with sertraline. The risk of SS or NMS with SSRIs is increased with concomitant use of serotonergic drugs (including triptans), with drugs which impair metabolism of serotonin (including MAOIs), antipsychotics and other dopamine antagonists. Patients should be monitored for the emergence of signs and symptoms of SS or NMS syndrome.

Switching from Selective Serotonin Reuptake Inhibitors (SSRIs), antidepressants or anti-obsessional drugs

There is limited controlled experience regarding the optimal timing of switching from SSRIs, antidepressants or anti-obsessional drugs to sertraline. Care and prudent medical judgment should be exercised when switching, particularly from long-acting agents such as fluoxetine.

Other serotonergic drugs e.g. tryptophan, fenfluramine and 5-HT agonists

Co-administration of Sertraline with other drugs which enhance the effects of serotonergic neurotransmission such as tryptophan or fenfluramine or 5-HT agonists, or the herbal medicine, St John's Wort (hypericum perforatum), should be undertaken with caution and avoided whenever possible due to the potential for a pharmacodynamic interaction.

Activation of hypomania or mania

Manic/hypomanic symptoms have been reported to emerge in a small proportion of patients treated with marketed antidepressant and anti-obsessional drugs, including Sertraline. Therefore Sertraline should be used with caution in patients with a history of mania/hypomania. Close surveillance by the physician is required. Sertraline should be discontinued in any patient entering a manic phase.

Schizophrenia

Psychotic symptoms might become aggravated in schizophrenic patients.

Seizures

Seizures may occur with sertraline therapy: Sertraline should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. Sertraline should be discontinued in any patient who develops seizures.

Suicide/suicidal thoughts/suicide attempts or clinical worsening

Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery. Other psychiatric conditions, for which Sertraline is prescribed, can also be associated with an increased risk of suicide-related events. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders.
Patients with a history of suicide related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.
Close supervision of patients and in particular those at high risk should accompany drug therapy especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Children

The safety and effectiveness of Sertraline in children have not been fully established.

Abnormal bleeding/Haemorrhage

There have been reports of cutaneous bleeding abnormalities such as ecchymoses and purpura and other hemorrhagic events such as gastrointestinal or gynaecological bleeding, with SSRIs. Caution is advised in patients taking SSRIs, particularly in concomitant use with drugs known to affect platelet function (e.g. anticoagulants, atypical antipsychotics and phenothiazines, most tricyclic antidepressants, acetylsalicylic acid and non-steroidal anti-inflammatory drugs (NSAIDs)) as well as in patients with a history of bleeding disorders (see drug interactions above).

Hyponatraemia

Hyponatraemia may occur as a result of treatment with SSRIs or SNRIs including Sertraline. In many cases, hyponatraemia appears to be the result of a syndrome of inappropriate antidiuretic hormone secretion (SIADH). Cases of serum sodium levels lower than 110 mmol/L have been reported.
Elderly patients may be at greater risk of developing hyponatraemia with SSRIs and SNRIs. Also patients taking diuretics or who are otherwise volume-depleted may be at greater risk . Discontinuation of Sertraline should be considered in patients with symptomatic hyponatraemia and appropriate medical intervention should be instituted. Signs and symptoms of hyponatraemia include headache, difficulty concentrating, memory impairment, confusion, weakness and unsteadiness which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death.

Withdrawal symptoms seen on discontinuation of sertraline treatment

Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see undesirable effects).
The risk of withdrawal symptoms may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction. Dizziness, sensory disturbances (including paraesthesia), sleep disturbances (including insomnia and intense dreams), agitation or anxiety, nausea and/or vomiting, tremor and headache are the most commonly reported reactions. Generally these symptoms are mild to moderate; however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose.

Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that Sertraline should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient's needs.

Akathisia/psychomotor restlessness

The use of Sertraline has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness and need to move often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Hepatic impairment

Sertraline is extensively metabolized by the liver. The use of Sertraline in patients with hepatic disease must be approached with caution. If Sertraline is administered to patients with hepatic impairment, a lower or less frequent dose should be considered. Sertraline should not be used in patients with severe hepatic impairment.

Renal impairment

Sertraline is extensively metabolized, and excretion of unchanged drug in urine is a minor route of elimination. Sertraline dosing does not have to be adjusted based on the degree of renal impairment.

Use in elderly

SSRIs or SNRIs including Sertraline have however been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event.

Diabetes

In patients with diabetes, treatment with an SSRI may alter glycaemic control, possibly due to improvement of depressive symptoms. Glycaemic control should be carefully monitored in patients receiving Sertraline and the dosage of insulin and/or concomitant oral hypoglycemic medicinal products may be needed to be adjusted.

Electroconvulsive therapy

There are no clinical studies establishing the risks or benefits of the combined use of ECT and Sertraline.

Effects on ability to drive and use machines

Clinical pharmacology studies have shown that Sertraline has no effect on psychomotor performance. However, as psychotropic drugs may impair the mental or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery, the patient should be cautioned accordingly.

Suicidality in Children and Adolescents

- Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders.
- Anyone considering the use of an antidepressant in a child or adolescent for any clinical use must balance the risk of increased suicidality with the clinical need.
- Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior.
- Families and caregivers should be advised to closely observe the patient and to communicate with the prescriber.
- Sertraline is not approved for use in children.

Sexual dysfunction

Selective serotonin reuptake inhibitors (SSRIs)/ serotonin norepinephrine reuptake inhibitors (SNRIs) may cause symptoms of sexual dysfunction. There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs/SNRIs.

✧ PREGNANCY AND LACTATION#:

Pregnancy

No teratogenic effects were demonstrated in rats and rabbits receiving 20 and 10 times the maximum daily human mg/Kg dose, respectively. Adequate and well controlled studies in humans have not been done. Sisalon should be used during pregnancy if clearly needed.

Lactation

There is no data available on the secretion of Sertraline in breast milk, hence use in nursing mothers is not recommended.

^Observational data indicate an increased risk (less than 2-fold) of postpartum hemorrhage following SSRI/SNRI exposure within the month prior to birth.

✧ SIDE EFFECT#:

Adverse effects that occurred significantly more frequently with sertraline than with placebo in multiple-dose studies for depression were:

Gastrointestinal Disorders: Diarrhea/loose stools, dry mouth, dyspepsia and nausea.

Metabolism and Nutrition Disorders: Anorexia.

Nervous System Disorders: Dizziness, somnolence and tremor.

Psychiatric Disorders: Insomnia.

Reproductive System and Breast Disorders: Sexual dysfunction (principally ejaculatory delay in males).

Skin and Subcutaneous Tissue Disorders: Increased sweating.

The side effect profile commonly observed in double-blind, placebo-controlled studies in patients with OCD, panic disorder, PTSD, and social phobia was similar with patients with depression.

Post-marketing Data

Blood and Lymphatic System Disorders: Leucopenia and thrombocytopenia.

Cardiac Disorders: Palpitations and tachycardia.

Ear and Labyrinth Disorders: Tinnitus.

Endocrine Disorders: Hyperprolactinemia, hypothyroidism and syndrome of inappropriate ADH secretion. (SIADH).

Eye Disorders: Mydriasis and abnormal vision.

^^Gastrointestinal Disorders: Abdominal pain, constipation, pancreatitis, vomiting and microscopic colitis/colitis microscopic.

General Disorders and Administration Site Conditions: Asthenia, chest pain, peripheral edema, fatigue, fever and malaise.

Hepatobiliary Disorders: Serious liver events (including hepatitis, jaundice and liver failure) and asymptomatic elevations in serum transaminases (SGOT and SGPT).

Immune System Disorders: Allergic reaction, allergy and anaphylactoid reaction.

Investigations: Abnormal clinical laboratory results, altered platelet function, increased serum cholesterol, weight decrease and increase.

Metabolism and Nutrition Disorders: Appetite increased and hyponatremia.

Musculoskeletal and Connective Tissue Disorders: Arthralgia and muscle cramps.

Nervous System Disorders: Coma, convulsions, headache, hypoesthesia, migraine, movement disorders (including extrapyramidal symptoms eg, hyperkinesia, hypertonia, teeth grinding or gait abnormalities), involuntary muscle contraction, paresthesia and syncope. Also reported were signs and symptoms associated with serotonin syndrome: In cases associated with concomitant use of serotonergic drugs that included agitation, confusion, diaphoresis, diarrhea, fever, hypertension, rigidity and tachycardia.

Psychiatric Disorders: Aggressive reaction, agitation, anxiety, depressive symptoms, euphoria, hallucination, decreased female and male libido, paroniria and psychosis.

Renal and Urinary Disorders: Urinary incontinence and retention.

Reproductive System and Breast Disorders: Galactorrhea, gynecomastia, menstrual irregularities and priapism.

Respiratory, Thoracic and Mediastinal Disorders: Bronchospasm and yawning.

Skin and Subcutaneous Tissue Disorders: Alopecia, angioedema, face edema, periorbital edema, photosensitivity skin reaction, pruritus, purpura, rash (including rare reports of serious exfoliative skin disorders eg, Stevens-Johnson syndrome and epidermal necrolysis) and urticaria.

Vascular Disorders: Abnormal bleeding (eg, epitaxis, gastrointestinal bleeding or hematuria), hot flushes and hypertension.

Others: Symptoms following discontinuation of sertraline have been reported eg, agitation, anxiety, dizziness, headache, nausea and paresthesia.

✧ CONTRAINDICATION:

- Hypersensitivity to the active substance or any of the excipients.
- Concomitant treatment with irreversible monoamine oxidase inhibitors (MAOIs) is contraindicated due to the risk of serotonin syndrome with symptoms such as agitation, tremor and hyperthermia. Sertraline must not be initiated for at least 14 days after discontinuation of treatment with an irreversible MAOI. Sertraline must be discontinued for at least 7 days before starting treatment with an irreversible MAOI.
- Concomitant intake of Pimozide is contraindicated.

✧ DRUG INTERACTION#:

Cases of serious sometimes fatal reactions have been reported in patients receiving Sertraline. In combination with monoamine oxidase inhibitor (MAOI), symptoms of a drug interaction between an SSRI and a MAOI include hyperthermia, rigidity, myoclonus autonomic instability with possible rapid fluctuations of vital signs, mental status changes that include confusion, irritability and extreme agitation progressing to delirium and coma. Some cases presented with features resembling neuroleptic malignant syndrome. Therefore, Sertraline should not be used in combination with a MAOI or within 14 days of discontinuing treatment with a MAOI. Similarly, at least 14 days should be allowed after stopping Sertraline before starting a MAOI.

Concurrent use of intravenous Diazepam with Sertraline may reduce the clearance and prolong the half-life of Diazepam.

Caution is recommended during concurrent use of Digitoxin and Warfarin with Sertraline because of possible displacement of either medication from protein binding sites. This may lead to increase plasma concentration and increased risk of adverse effects. Prothrombin time should be carefully monitored when Sertraline therapy is initiated or stopped in patients taking Warfarin. Drugs metabolized with cytochrome P450 2D6, Sertraline inhibits the biochemical activity of the drug metabolizing isozyme P450 2D6 and, thus may increase the plasma concentration of co-administered drugs, (which are metabolized by P450 2D6) such as tricyclic antidepressants and Type IC antiarrythmics, Propafenone, and Flecainide.

Dose reduction may be required.

Nonetheless, it is recommended that plasma lithium levels be monitored following initiations of Sertraline therapy with appropriate adjustment to the lithium dose.

✧ OVERDOSE AND TREATMENT:

Toxicity

Sertraline has a margin of safety dependent on patient population and/or concomitant medication. Deaths have been reported involving overdoses of Sertraline, alone or in combination with other drugs and/or alcohol. Therefore, any overdosage should be medically treated aggressively.

Symptoms

Symptoms of overdose include serotonin-mediated side effects such as somnolence, gastrointestinal disturbances (such as nausea and vomiting), tachycardia, tremor, agitation and dizziness. Less frequently reported was coma.

Treatment

There are no specific antidotes to Sertraline. Establish and maintain an airway and ensure adequate oxygenation and ventilation, if necessary. Activated charcoal, which may be used with a cathartic, may be as or more effective than lavage, and should be considered in treating overdose. Induction of emesis is not recommended. Cardiac and other vital sign monitoring is recommended, along with general symptomatic and supportive measures.

Due to the large volume of distribution of Sertraline, forced diuresis, dialysis, hemoperfusion and exchange transfusion are unlikely to be of benefit.

Sertraline overdose may prolong the QT-interval, and ECG-monitoring is recommended in all ingestions of Sertraline overdoses.

✧ STORAGE:

Store at temperature of not more than 30ºC.

✧ DOSAGE FORM AND PACKAGING AVAILABLE:

50 mg Tablet, Blister 10x10's

✧ DATE OF REVISION:

October 17, 2025

Manufactured by:
UNISON LABORATORIES CO., LTD.
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