Front Size should be adjusted by the Vendor/ CMO as per available tooling. Back

Sabert™

(S e r t r a l i n e) Tablet

سیبرٹ

COMPOSITION:
Sabert Tablet 50 mg:
Each film coated tablet contains:
Sertraline HCl equivalent to Sertraline ..... 50 mg.

Product Specs.: USP

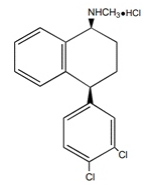
Sabert Tablet 100 mg:
Each film coated tablet contains:
Sertraline HCl equivalent to Sertraline ..... 100 mg.

Product Specs.: USP

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS
- Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients.
- Closely monitor for clinical worsening and emergence of suicidal thoughts and behaviours.

DESCRIPTION:
Sertraline is indicated for the treatment of symptoms of depressive illness including accompanying symptoms of anxiety. Continuation of Sertraline therapy is also effective in preventing relapse of the initial episode of depression or reoccurrence of further depressive episodes including accompanying symports of anxiety. Sertraline is also indicated for the treatment of obsessive-compulsive disorder (OCD). Following initial response, Sertraline has been associated with the sustained efficacy, safety, and tolerability in up to 2 years treatment of OCD. Sertraline is not indicated for use in children and adolescent under the age of 18 years with Major Depressive Disorder. In particular; controlled clinical studies failed to demonstrate efficacy and do not support the use of Sertraline in the treatment of children and adolescent with Major Depressive Disorder.

CLINICAL PHARMACOLOGY:
Having the below molecular structure, Sertraline potentiates serotonergic activity in the central nervous system through inhibition of neuronal reuptake of serotonin (5-HT).



Pharmacodynamics: Sertraline is a potent and selective inhibitor of neuronal serotonin reuptake and has only very weak effects on norepinephrine and dopamine neuronal reuptake. In vitro studies have shown that Sertraline has no significant affinity for adrenergic (alpha1, alpha2, beta), cholinergic, GABA, dopaminergic, histaminergic, serotonergic (5HT1A, 5HT1B, 5HT2), or benzodiazepine receptors; antagonism of such receptors has been hypothesized to be associated with various anticholinergic, sedative, and cardiovascular effects for other psychotropic drugs. The chronic administration of Sertraline was found in animals to down regulate brain norepinephrine receptors, as has been observed with other drugs effective in the treatment of major depressive disorder. Sertraline does not inhibit monoamine oxidase.
Pharmacokinetics: Mean peak plasma concentrations (Cmax) of sertraline occurred between 4.5 to 8.4 hours post-dosing. The average terminal elimination half-life of plasma sertraline is about 26 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. Administration with food causes a small increase in Cmax and AUC.
Metabolism: Sertraline undergoes extensive first pass metabolism. The principal initial pathway of metabolism for sertraline is N-demethylation. N-desmethylsertraline has a plasma terminal elimination half-life of 62 to 104 hours. Both in vitro biochemical and in vivo pharmacological testing have shown N-desmethylsertraline to be substantially less active than sertraline. Both sertraline and N-desmethylsertraline undergo oxidative deamination and subsequent reduction, hydroxylation, and glucuronide conjugation. Desmethylsertraline exhibits time-related, dose dependent increases in AUC (0-24-hour), Cmax and Cmin, with about a 5- to 9-fold increase in these pharmacokinetic parameters between day 1 and day 14.
Pediatric pharmacokinetics: Studies in paediatric population show higher plasma levels in the 6–12 year old group which were largely attributable to patients with lower body weights. No gender associated differences were observed. By comparison, a group of 22 separately studied adults between 18 and 45 years of age (11 male, 11 female) received 30 days of 200 mg/day Sertraline and exhibited a mean Sertraline AUC (0-24 hr) of 2570 ng-hr/mL, mean Cmax of 142 ng/mL, and mean half-life of 27.2 hr. Relative to the adults, both the 6–12-year-olds and the 13–17-year-olds showed about 22% lower AUC (0-24 hr) and Cmax values when plasma concentration was adjusted for weight. These data suggest that pediatric patients metabolize Sertraline with slightly greater efficiency than adults. Nevertheless, lower doses may be advisable for pediatric patients given their lower body weights, especially in very young patients, in order to avoid excessive plasma levels.

INDICATIONS:
Major depressive disorder. Sertraline is indicated for the treatment of major depressive disorder in adults. The efficacy of Sertraline in the treatment of a major depressive episode was established in six-to-eight-week controlled trials of adult outpatients whose diagnoses corresponded most closely to the DSM-III category of major depressive disorder. A major depressive episode implies a prominent and relatively persistent depressed or dysphoric mood that usually interferes with daily functioning (nearly every day for at least 2 weeks); it should include at least 4 of the following 8 symptoms: change in appetite, change in sleep, psychomotor agitation or retardation, loss of interest in usual activities or decrease in sexual drive, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, and a suicide attempt or suicidal ideation. The antidepressant action of Sertraline in hospitalized depressed patients has not been adequately studied. The efficacy of Sertraline in maintaining an antidepressant response for up to 44 weeks following 8 weeks of open-label acute treatment (52 weeks total) was demonstrated in a placebo-controlled trial. The usefulness of the drug in patients receiving Sertraline for extended periods should be reevaluated periodically.
Obsessive-Compulsive disorder. Sertraline is indicated for the treatment of obsessions and compulsions in patients with obsessive-compulsive disorder (OCD), as defined in the DSM-III-R; i.e., the obsessions or compulsions cause marked distress, are time-consuming, or significantly interfere with social or occupational functioning. 10 The efficacy of SERTRALINE was established in 12-week trials with obsessive-compulsive outpatients having diagnoses of obsessive-compulsive disorder as defined according to DSM-III or DSM-III-R criteria. Obsessive-compulsive disorder is characterized by recurrent and persistent ideas, thoughts, impulses, or images (obsessions) that are ego-dystonic and/or repetitive, purposeful, and intentional behaviors (compulsions) that are recognized by the person as excessive or unreasonable. The efficacy of Sertraline in maintaining a response, in patients with OCD who responded during a 52-week treatment phase while taking SERTRALINE and were then observed for relapse during a period of up to 28 weeks, was demonstrated in a placebo-controlled trial. Nevertheless, the physician who elects to use SERTRALINE for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.
Panic disorder – Sertraline is indicated for the treatment of panic disorder in adults, with or without agoraphobia, as defined in DSM-IV. The efficacy of SERTRALINE was established in three 10–12-week trials in adult panic disorder patients whose diagnoses corresponded to the DSM-III-R category of panic disorder. The efficacy of Sertraline in maintaining a response, in adult patients with panic disorder who responded during a 52-week treatment phase while taking SERTRALINE and were then observed for relapse during a period of up to 28 weeks, was demonstrated in a placebo-controlled trial. Nevertheless, the physician who elects to use SERTRALINE for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.
Post-traumatic stress disorder (PTSD) – SERTRALINE (Sertraline hydrochloride) is indicated for the treatment of posttraumatic stress disorder in adults. The efficacy of Sertraline in maintaining a response in adult patients with PTSD for up to 28 weeks following 24 weeks of open-label treatment was demonstrated in a placebo-controlled trial. Nevertheless, the physician who elects to use SERTRALINE for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.
Premenstrual dysphoric disorder (PMDD) – Sertraline is indicated for the treatment of premenstrual dysphoric disorder (PMDD) in adults. The efficacy of Sertraline in the treatment of PMDD was established in 2 placebo-controlled trials of female adult outpatients treated for 3 menstrual cycles who met criteria for the DSM-IIIR/IV category of PMDD. The effectiveness of Sertraline in long-term use, that is, for more than 3 menstrual cycles, has not been systematically evaluated in controlled trials. Therefore, the physician who elects to use SERTRALINE for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.
Social anxiety disorder – SERTRALINE (Sertraline hydrochloride) is indicated for the treatment of social anxiety disorder, also known as social phobia in adults. The efficacy of Sertraline in the treatment of social anxiety disorder was established in two placebo-controlled trials of adult outpatients with a diagnosis of social anxiety disorder as defined by DSM-IV criteria. The efficacy of Sertraline in maintaining a response in adult patients with social anxiety disorder for up to 24 weeks following 20 weeks of SERTRALINE treatment was demonstrated in a placebo-controlled trial. Physicians who prescribe SERTRALINE for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient.

DOSAGE AND ADMINISTRATION:
Initial Treatment Dosage for Adults:
Major depressive disorder and obsessive compulsive disorder. SERTRALINE treatment should be administered at a dose of 50 mg once daily. Maximum dosage is 200 mg per day.
panic disorder, Posttraumatic stress disorder and social anxiety disorder: SERTRALINE treatment should be initiated with a dose of 25 mg once daily. After one week, the dose should be increased to 50 mg once daily. Patients not responding to a 50 mg dose may benefit from dose increases up to a maximum of 200 mg/day.
Given the 24-hour elimination half-life of SERTRALINE, dose changes should not occur at intervals of less than 1 week.
Premenstrual dysphoric disorder. SERTRALINE treatment should be initiated with a dose of 50 mg/day, either daily throughout the menstrual cycle or limited to the luteal phase of the menstrual cycle, depending on physician assessment. While a relationship between dose and effect has not been established for PMDD, patients were dosed in the range of 50-150 mg/day with dose increases at the onset of each new menstrual cycle (see Clinical Trials under CLINICAL PHARMACOLOGY). Patients not responding to a 50 mg/day dose may benefit from dose increases (at 50 mg increments/menstrual cycle) up to 150 mg/day when dosing daily throughout the menstrual cycle, or 100 mg/day when dosing 38 during the luteal phase of the menstrual cycle. If a 100 mg/day dose has been established with luteal phase dosing, a 50 mg/day titration step for three days should be utilized at the beginning of each luteal phase dosing period.
Post-traumatic stress disorder. It is generally agreed that PTSD requires several months or longer of sustained pharmacological therapy beyond response to initial treatment. Systematic evaluation of SERTRALINE has demonstrated that its efficacy in PTSD is maintained for periods of up to 28 weeks following 24 weeks of treatment at a dose of 50-200 mg/day. It is not known whether the dose of SERTRALINE needed for maintenance treatment is identical to the dose needed to achieve an initial response. Patients should be periodically reassessed to determine the need for maintenance treatment.
Social anxiety disorder: Social anxiety disorder is a chronic condition that may require several months or longer of sustained pharmacological therapy beyond response to initial treatment. Systematic evaluation of SERTRALINE has demonstrated that its efficacy in social anxiety disorder is maintained for periods of up to 24 weeks following 20 weeks of treatment at a dose of 50-200 mg/day. Dosage adjustments should be made to maintain patients on the lowest effective dose and patients should be periodically reassessed to determine the need for long-term treatment.
Obsessive compulsive disorder and panic disorder. Systematic evaluation of continuing SERTRALINE for periods of up to 28 weeks in patients with OCD and Panic Disorder who have responded while taking SERTRALINE during initial treatment phases of 24 to 52 weeks of treatment at a dose range of 50-200 mg/day has demonstrated a benefit of such maintenance treatment. It is not known whether the dose of SERTRALINE needed for maintenance treatment is identical to the dose needed to achieve an initial response. Nevertheless, patients should be periodically reassessed to determine the need for maintenance treatment.
Premenstrual dysphoric disorder. The effectiveness of SERTRALINE in long-term use, that is, for more than 3 menstrual cycles, has not been systematically evaluated in controlled trials. However, as women commonly report that symptoms worsen with age until relieved by the onset of menopause, it is reasonable to consider continuation of a responding patient. Dosage adjustments, which may include changes between dosage regimens (e.g., daily throughout the menstrual cycle versus during the luteal phase of the menstrual cycle), may be needed to maintain the patient on the lowest effective dosage and patients should be periodically reassessed to determine the need for continued treatment. Switching Patients to or from a Monoamine Oxidase Inhibitor–At least 14 days should elapse between discontinuation of an MAOI and initiation of therapy with SERTRALINE. In addition, at least 14 days should be allowed after stopping SERTRALINE before starting an MAOI.
Dosage for Pediatric Population (Children and Adolescents): Obsessive Compulsive Disorder: SERTRALINE treatment should be initiated with a dose of 25 mg once daily in children (ages 6-12) and at a dose of 50 mg once daily in adolescents (ages 13-17). While a relationship between dose and effect has not been established for OCD, patients were dosed in a range of 25-200 mg/day in the clinical trials demonstrating the effectiveness of SERTRALINE for pediatric patients (6-17 years) with OCD. Patients not responding to an initial dose of 25 or 50 mg/day may benefit from dose increases up to a maximum of 200 mg/day. For children with OCD, their generally lower body weights compared to adults should be taken into consideration in advancing the dose, in order to avoid excess dosing. Given the 24-hour elimination half-life of SERTRALINE, dose changes should not occur at intervals of less than 1 week. SERTRALINE should be administered once daily, either in the morning or evening.
SERTRALINE IS NOT INDICATED FOR USE IN CHILDREN AND ADLOESCENTS UNDER THE AGE OF 18 YEARS WITH MAJOR DEPRESSIVE DISORDER

WARNINGS & PRECAUTIONS:
Antidepressants increased the risk of suicidal thoughts and behavior in pediatric and young adult patients in short term studies. Closely monitor all antidepressant-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors.
Suicidal thoughts and behaviors in pediatric and young adult patients: Both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table 1.

Table 1

Age Range	Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated
	Increases Compared to Placebo
<18	14 additional cases
18-24	5 additional cases
	Decreases Compared to Placebo
25-64	1 fewer case
≥65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression. All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms. Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for SERTRALINE should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.
Serotonin syndrome or neuroleptic malignant syndrome: like Reactions The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including Sertraline treatment, but particularly with concomitant use of serotonergic drugs (including triptans) with drugs which impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Serotonin syndrome, in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms. The concomitant use of Sertraline with MAOIs intended to treat depression is contraindicated. If concomitant treatment of Sertraline with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Sertraline with serotonin precursors (such as tryptophan) is not recommended. Treatment with Sertraline and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated.
Increased risk of bleeding: Drugs that interfere with serotonin reuptake inhibition, including SERTRALINE, increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), other antiplatelet drugs, warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to drugs that interfere with serotonin reuptake have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages. Inform patients of the increased risk of bleeding associated with the concomitant use of SERTRALINE and antiplatelet agents or anticoagulants. For patients taking warfarin, carefully monitor the international normalized ratio.
Activation of mania or hypomania: In patients with bipolar disorder, treating a depressive episode with SERTRALINE or another antidepressant may precipitate a mixed/manic episode. In controlled clinical trials, patients with bipolar disorder were generally excluded; however, symptoms of mania or hypomania were reported in 0.4% of patients treated with SERTRALINE. Prior to initiating treatment with SERTRALINE, screen patients for any personal or family history of bipolar disorder, mania, or hypomania.
Discontinuation syndrome: Adverse reactions after discontinuation of serotonergic antidepressants, particularly after abrupt discontinuation, include: nausea, sweating, dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), tremor, anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible.
Others: seizures, closed angle glaucoma, hyponatremia.

SPECIAL POPULATIONS:
Dosage for hepatically impaired patients: The use of Sertraline in patients with liver disease should be approached with caution. The effects of Sertraline in patients with moderate and severe hepatic impairment have not been studied. If Sertraline is administered to patients with liver impairment, a lower or less frequent dose should be used.
Treatment of pregnant women during the third trimester. Neonates exposed to SERTRALINE and other SSRIs or SNRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. When treating pregnant women with SERTRALINE during the third trimester, the physician should carefully consider the potential risks and benefits of treatment. The physician may consider tapering Sertraline in the third trimester.
Geriatric use: No overall differences in the pattern of adverse reactions were observed in the geriatric clinical trial subjects relative to those reported in younger subjects, and other reported experience has not identified differences in safety patterns between the elderly and younger subjects. As with all medications, greater sensitivity of some older individuals cannot be ruled out. The overall profile of adverse events was generally similar. Urinary tract infection was the only adverse event not appearing and reported at an incidence of at least 2% and at a rate greater than placebo in placebo-controlled trials. SSRIS and SNRIs, including SERTRALINE have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event.

CONTRAINDICATIONS:
SERTRALINE is contraindicated in patients:
- Taking, or within 14 days of stopping, MAOIs, (including the MAOIs linezolid and intravenous methylene blue) because of an increased risk of serotonin syndrome.
- Taking pimozide.
- With known hypersensitivity to Sertraline (e.g., anaphylaxis, angioedema).

DRUG INTERACTIONS:
Sertraline can have clinically significant drug interactions with MAO inhibitors (selegiline, tranylcypromine, isocarboxazid, phenelzine, linezolid, methylene blue), pimozide, serotonergic drugs (SNRIs, triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's Wort), apirin, heparin, warfarin and clopidogrel, phenytoin and drugs metabolized by CYP2D6 including propafenone, flecainide, atomoxetine, desipramine, dextromethorphan, metoprolol, nebivolol, perphenazine, thoridazine, tolterodine, venlafaxine.

ADVERSE REACTIONS:
Most common adverse reactions (>5% and twice placebo) in pooled placebo controlled MDD, OCD, PD, PTSD, SAD and PMDD clinical trials were nausea, diarrhea/loose stool, tremor, dyspepsia, decreased appetite, hyperhidrosis, ejaculation failure, and decreased libido.
The following adverse reactions are reported frequently:
- Hypersensitivity reactions to Sertraline
- QT prolongation and ventricular arrhythmias when taken with pimozide
- Suicidal thoughts and behaviors
- Serotonin syndrome
- Increased risk of bleeding
- Activation of mania/hypomania
- Discontinuation syndrome
- Seizures
- Angle-closure glaucoma
- Hyponatremia

General: Frequent: back pain, asthenia, malaise, weight increase; **Infrequent:** fever, rigors, generalized edema; **Rare:** face edema, aphthous stomatitis.
Male and female sexual dysfunction: Although changes in sexual desire, sexual performance and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that selective serotonin reuptake inhibitors (SSRIs) can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance and satisfaction are 33 difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling, are likely to underestimate their actual incidence. There are no adequate and well-controlled studies examining sexual dysfunction with Sertraline treatment. Priapism has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects.
Other adverse events in pediatric patients: In over 600 pediatric patients treated with SERTRALINE the overall profile of adverse events was generally similar to that seen in adult studies. However, the following adverse events, from controlled trials were reported at an incidence of at least 2% and occurred at a rate of at least twice the placebo rate (N=281 patients treated with SERTRALINE: fever, hyperkinesia, urinary incontinence, aggressive reaction, sinusitis, epistaxis and purpura.
Post marketing experience: The following adverse reactions have been identified during post approval use of Sertraline. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
- Bleeding or clotting disorders - increased coagulation times (altered platelet function) Cardiac disorders – AV block, bradycardia, atrial arrhythmias, QT-interval prolongation, ventricular tachycardia (including Torsade de Pointes)
- Endocrine disorders - gynecomastia, hyperprolactinemia, menstrual irregularities, SIADH Eye disorders - blindness, optic neuritis, cataract Hepatobiliary disorders – severe liver events (including hepatitis, jaundice, liver failure with some fatal outcomes), pancreatitis Hemic and Lymphatic – agranulocytosis, aplastic anemia and pancytopenia, leukopenia, thrombocytopenia, lupus-like syndrome, serum sickness Immune system disorders – angioedema.
- Metabolism and nutrition disorders – hyponatremia, hyperglycemia
- Nervous system disorders - serotonin syndrome, extrapyramidal symptoms (including akathisia and dystonia), oculogyric crisis Psychiatric disorders – psychosis, enuresis, paroniria
- Renal and urinary disorders - acute renal failure
- Respiratory, thoracic and mediastinal disorders - pulmonary hypertension
- Skin and subcutaneous tissue disorders - photosensitivity skin reaction and other severe cutaneous reactions, which potentially can be fatal, such as Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN)
- Vascular disorders - cerebrovascular spasm (including reversible cerebral vasoconstriction syndrome and Call-Fleming syndrome), vasculitis.

OVERDOSAGE:
The most common signs and symptoms associated with non-fatal Sertraline hydrochloride overdosage were somnolence, vomiting, tachycardia, nausea, dizziness, agitation and tremor. Other important adverse events reported with Sertraline hydrochloride overdose (single or multiple drugs) include bradycardia, bundle branch block, coma, convulsions, delirium, hallucinations, hypertension, hypotension, manic reaction, pancreatitis, QT-interval prolongation, serotonin syndrome, stupor and syncope.
Overdose management: Treatment should consist of general measures employed in the management of overdosage with any antidepressant. Ensure an adequate airway, oxygenation and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion, or in symptomatic patients. Activated charcoal should be administered. Due to large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion and exchange transfusion are unlikely to be of benefit. No specific antidotes for Sertraline are known. In managing overdosage, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center on the treatment of any overdose.

INSTRUCTIONS:
- Store below 30ºC.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
Sabert Tablet 50 mg : Pack of 3 x 10 tablets.
Sabert Tablet 100 mg : Pack of 2 x 10 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
WnsFeild Pharmaceuticals.
Plot # 122, Block A, Phase V, Industrial Estate, Hattar, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

Marketed by:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

zoom view

Front

Sabert™

(S e r t r a l i n e) Tablet

سیبرٹ

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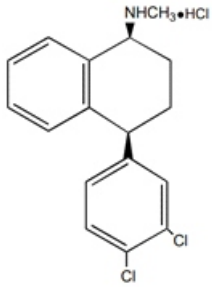
- Closely monitor for clinical worsening and emergence of suicidal thoughts and behaviours.

DESCRIPTION:
Sertraline is indicated for the treatment of symptoms of depressive illness including accompanying symptoms of anxiety. Continuation of Sertraline therapy is also effective in preventing relapse of the initial episode of depression or reoccurrence of further depressive episodes including accompanying symports of anxiety. Sertraline is also indicated for the treatment of obsessive-compulsive disorder (OCD). Following initial response, Sertraline has been associated with the sustained efficacy, safety, and tolerability in up to 2 years treatment of OCD. Sertraline is not indicated for use in children and adolescent under the age of 18 years with Major Depressive Disorder. In particular; controlled clinical studies failed to demonstrate efficacy and do not support the use of Sertraline in the treatment of children and adolescent with Major Depressive Disorder.

CLINICAL PHARMACOLOGY:
Having the below molecular structure, Sertraline potentiates serotonergic activity in the central nervous system through inhibition of neuronal reuptake of serotonin (5-HT).



Pharmacodynamics: Sertraline is a potent and selective inhibitor of neuronal serotonin reuptake and has only very weak effects on norepinephrine and dopamine neuronal reuptake. In vitro studies have shown that Sertraline has no significant affinity for adrenergic (alpha1, alpha2, beta), cholinergic, GABA, dopaminergic, histaminergic, serotonergic (5HT1A, 5HT1B, 5HT2), or benzodiazepine receptors; antagonism of such receptors has been hypothesized to be associated with various anticholinergic, sedative, and cardiovascular effects for other psychotropic drugs. The chronic administration of Sertraline was found in animals to down regulate brain norepinephrine receptors, as has been observed with other drugs effective in the treatment of major depressive disorder. Sertraline does not inhibit monoamine oxidase.
Pharmacokinetics: Mean peak plasma concentrations (Cmax) of sertraline occurred between 4.5 to 8.4 hours post-dosing. The average terminal elimination half-life of plasma sertraline is about 26 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. Administration with food causes a small increase in Cmax and AUC.
Metabolism: Sertraline undergoes extensive first pass metabolism. The principal initial pathway of metabolism for sertraline is N-demethylation. N-desmethylsertraline has a plasma terminal elimination half-life of 62 to 104 hours. Both in vitro biochemical and in vivo pharmacological testing have shown N-desmethylsertraline to be substantially less active than sertraline. Both sertraline and N-desmethylsertraline undergo oxidative deamination and subsequent reduction, hydroxylation, and glucuronide conjugation. Desmethylsertraline exhibits time-related, dose dependent increases in AUC (0-24-hour), Cmax and Cmin, with about a 5- to 9-fold increase in these pharmacokinetic parameters between day 1 and day 14.
Pediatric pharmacokinetics: Studies in paediatric population show higher plasma levels in the 6–12 year old group which were largely attributable to patients with lower body weights. No gender associated differences were observed. By comparison, a group of 22 separately studied adults between 18 and 45 years of age (11 male, 11 female) received 30 days of 200 mg/day Sertraline and exhibited a mean Sertraline AUC (0-24 hr) of 2570 ng-hr/mL, mean Cmax of 142 ng/mL, and mean half-life of 27.2 hr. Relative to the adults, both the 6–12-year-olds and the 13–17-year-olds showed about 22% lower AUC (0-24 hr) and Cmax values when plasma concentration was adjusted for weight. These data suggest that pediatric patients metabolize Sertraline with slightly greater efficiency than adults. Nevertheless, lower doses may be advisable for pediatric patients given their lower body weights, especially in very young patients, in order to avoid excessive plasma levels.

INDICATIONS:
Major depressive disorder: Sertraline is indicated for the treatment of major depressive disorder in adults. The efficacy of Sertraline in the treatment of a major depressive episode was established in six-to-eight-week controlled trials of adult outpatients whose diagnoses corresponded most closely to the DSM-III category of major depressive disorder. A major depressive episode implies a prominent and relatively persistent depressed or dysphoric mood that usually interferes with daily functioning (nearly every day for at least 2 weeks); it should include at least 4 of the following 8 symptoms: change in appetite, change in sleep, psychomotor agitation or retardation, loss of interest in usual activities or decrease in sexual drive, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, and a suicide attempt or suicidal ideation. The antidepressant action of Sertraline in hospitalized depressed patients has not been adequately studied. The efficacy of Sertraline in maintaining an antidepressant response for up to 44 weeks following 8

weeks of open-label acute treatment (52 weeks total) was demonstrated in a placebo-controlled trial. The usefulness of the drug in patients receiving Sertraline for extended periods should be reevaluated periodically.

Obsessive-Compulsive disorder: Sertraline is indicated for the treatment of obsessions and compulsions in patients with obsessive-compulsive disorder (OCD), as defined in the DSM-III-R; i.e., the obsessions or compulsions cause marked distress, are time-consuming, or significantly interfere with social or occupational functioning. 10 The efficacy of SERTRALINE was established in 12-week trials with obsessive-compulsive outpatients having diagnoses of obsessive-compulsive disorder as defined according to DSM-III or DSM-III-R criteria. Obsessive-compulsive disorder is characterized by recurrent and persistent ideas, thoughts, impulses, or images (obsessions) that are ego-dystonic and/or repetitive, purposeful, and intentional behaviors (compulsions) that are recognized by the person as excessive or unreasonable. The efficacy of Sertraline in maintaining a response, in patients with OCD who responded during a 52-week treatment phase while taking SERTRALINE and were then observed for relapse during a period of up to 28 weeks, was demonstrated in a placebo-controlled trial. Nevertheless, the physician who elects to use SERTRALINE for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Panic disorder – Sertraline is indicated for the treatment of panic disorder in adults, with or without agoraphobia, as defined in DSM-IV. The efficacy of SERTRALINE was established in three 10–12-week trials in adult panic disorder patients whose diagnoses corresponded to the DSM-III-R category of panic disorder. The efficacy of Sertraline in maintaining a response, in adult patients with panic disorder who responded during a 52-week treatment phase while taking SERTRALINE and were then observed for relapse during a period of up to 28 weeks, was demonstrated in a placebo-controlled trial. Nevertheless, the physician who elects to use SERTRALINE for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Post-traumatic stress disorder (PTSD) – SERTRALINE (Sertraline hydrochloride) is indicated for the treatment of posttraumatic stress disorder in adults. The efficacy of Sertraline in maintaining a response in adult patients with PTSD for up to 28 weeks following 24 weeks of open-label treatment was demonstrated in a placebo-controlled trial. Nevertheless, the physician who elects to use SERTRALINE for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Premenstrual dysphoric disorder (PMDD) – Sertraline is indicated for the treatment of premenstrual dysphoric disorder (PMDD) in adults. The efficacy of Sertraline in the treatment of PMDD was established in 2 placebo-controlled trials of female adult outpatients treated for 3 menstrual cycles who met criteria for the DSM-IIIR/IV category of PMDD. The effectiveness of Sertraline in long-term use, that is, for more than 3 menstrual cycles, has not been systematically evaluated in controlled trials. Therefore, the physician who elects to use SERTRALINE for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Social anxiety disorder – SERTRALINE (Sertraline hydrochloride) is indicated for the treatment of social anxiety disorder, also known as social phobia in adults. The efficacy of Sertraline in the treatment of social anxiety disorder was established in two placebo-controlled trials of adult outpatients with a diagnosis of social anxiety disorder as defined by DSM-IV criteria. The efficacy of Sertraline in maintaining a response in adult patients with social anxiety disorder for up to 24 weeks following 20 weeks of SERTRALINE treatment was demonstrated in a placebo-controlled trial. Physicians who prescribe SERTRALINE for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient.

DOSAGE AND ADMINISTRATION:

Initial Treatment Dosage for Adults:

Major depressive disorder and obsessive compulsive disorder: SERTRALINE treatment should be administered at a dose of 50 mg once daily. Maximum dosage is 200 mg per day.

panic disorder, Posttraumatic stress disorder and social anxiety disorder: SERTRALINE treatment should be initiated with a dose of 25 mg once daily. After one week, the dose should be increased to 50 mg once daily. Patients not responding to a 50 mg dose may benefit from dose increases up to a maximum of 200 mg/day.

Given the 24-hour elimination half-life of SERTRALINE, dose changes should not occur at intervals of less than 1 week.

Premenstrual dysphoric disorder: SERTRALINE treatment should be initiated with a dose of 50 mg/day, either daily throughout the menstrual cycle or limited to the luteal phase of the menstrual cycle, depending on physician assessment. While a relationship between dose and effect has not been established for PMDD, patients were dosed in the range of 50-150 mg/day with dose increases at the onset of each new menstrual cycle (see Clinical Trials under CLINICAL PHARMACOLOGY). Patients not responding to a 50 mg/day dose may benefit from dose increases (at 50 mg increments/menstrual cycle) up to 150 mg/day when dosing daily throughout the menstrual cycle, or 100 mg/day when dosing 38 during the luteal phase of the menstrual cycle. If a 100 mg/day dose has been established with luteal phase dosing, a 50 mg/day titration step for three days should be utilized at the beginning of each luteal phase dosing period.

Post-traumatic stress disorder: It is generally agreed that PTSD requires several months or longer of sustained pharmacological therapy beyond response to initial treatment. Systematic evaluation of SERTRALINE has demonstrated that its efficacy in PTSD is maintained for periods of up to 28 weeks following 24 weeks of treatment at a dose of 50-200 mg/day. It is not known whether the dose of SERTRALINE needed for maintenance treatment is identical to the dose needed to achieve an initial response. Patients should be periodically reassessed to determine the need for maintenance treatment.

Social anxiety disorder: Social anxiety disorder is a chronic condition that may require several months or longer of sustained pharmacological therapy beyond response to initial treatment. Systematic evaluation of SERTRALINE has demonstrated that its efficacy in social anxiety disorder is maintained for periods of up to 24 weeks following 20 weeks of treatment at a dose of 50-200 mg/day. Dosage adjustments should be made to maintain patients on the lowest effective dose and patients should be periodically reassessed to determine the need for long-term treatment.

Obsessive compulsive disorder and panic disorder: Systematic evaluation of continuing SERTRALINE for periods of up to 28 weeks in patients with OCD and Panic Disorder who have responded while taking SERTRALINE during initial treatment phases of 24 to 52 weeks of treatment at a dose range of 50-200 mg/day has demonstrated a benefit of such maintenance treatment. It is not known whether the dose of SERTRALINE needed for maintenance treatment is identical to the dose needed to achieve an initial response. Nevertheless, patients should be periodically reassessed to determine the need for maintenance treatment.

Premenstrual dysphoric disorder: The effectiveness of SERTRALINE in long-term use, that is, for more than 3 menstrual cycles, has not been systematically evaluated in controlled trials. However, as women commonly report that symptoms worsen with age until relieved by the onset of menopause, it is reasonable to consider continuation of a responding patient. Dosage adjustments, which may include changes between dosage regimens (e.g., daily throughout the menstrual cycle versus during the luteal phase of the menstrual cycle), may be needed to maintain the patient on the lowest effective dosage and patients should be periodically reassessed to determine the need for continued treatment. Switching Patients to or from a Monoamine Oxidase Inhibitor–At least 14 days should elapse between discontinuation of an MAOI and initiation of therapy with SERTRALINE. In addition, at least 14 days should be allowed after stopping SERTRALINE before starting an MAOI.

Dosage for Pediatric Population (Children and Adolescents): Obsessive Compulsive Disorder: SERTRALINE treatment should be initiated with a dose of 25 mg once daily in children (ages 6-12) and at a dose of 50 mg once daily in adolescents (ages 13-17). While a relationship between dose and effect has not been established for OCD, patients were dosed in a range of 25-200 mg/day in the clinical trials demonstrating the effectiveness of SERTRALINE for pediatric patients (6-17 years) with OCD. Patients not responding to an initial dose of 25 or 50 mg/day may benefit from dose increases up to a maximum of 200 mg/day. For children with OCD, their generally lower body weights compared to adults should be taken into consideration in advancing the dose, in order to avoid excess dosing. Given the 24-hour elimination half-life of SERTRALINE, dose changes should not occur at intervals of less than 1 week. SERTRALINE should be administered once daily, either in the morning or evening.

SERTRALINE IS NOT INDICATED FOR USE IN CHILDREN AND ADLOESCENTS UNDER THE AGE OF 18 YEARS WITH MAJOR DEPRESSIVE DISORDER

WARNINGS & PRECAUTIONS:

Antidepressants increased the risk of suicidal thoughts and behavior in pediatric and young adult patients in short term studies. Closely monitor all antidepressant-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors.

Suicidal thoughts and behaviors in pediatric and young adult patients: Both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled

analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table 1.

Table 1

Age Range	Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated
	Increases Compared to Placebo
<18	14 additional cases
18-24	5 additional cases
	Decreases Compared to Placebo
25-64	1 fewer case
≥65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial

evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression. All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms. Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for SERTRALINE should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.

Serotonin syndrome or neuroleptic malignant syndrome: like Reactions The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including Sertraline treatment, but particularly with concomitant use of serotonergic drugs (including triptans) with drugs which impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Serotonin syndrome, in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms. The concomitant use of Sertraline with MAOIs intended to treat depression is contraindicated. If concomitant treatment of Sertraline with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Sertraline with serotonin precursors (such as tryptophan) is not recommended. Treatment with Sertraline and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated.

Increased risk of bleeding: Drugs that interfere with serotonin reuptake inhibition, including SERTRALINE, increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), other antiplatelet drugs, warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to drugs that interfere with serotonin reuptake have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages. Inform patients of the increased risk of bleeding associated with the concomitant use of SERTRALINE and antiplatelet agents or anticoagulants. For patients taking warfarin, carefully monitor the international normalized ratio.

Activation of mania or hypomania: In patients with bipolar disorder, treating a depressive episode with SERTRALINE or another antidepressant may precipitate a mixed/manic episode. In controlled clinical trials, patients with bipolar disorder were generally excluded; however, symptoms of mania or hypomania were reported in 0.4% of patients treated with SERTRALINE. Prior to initiating treatment with SERTRALINE, screen patients for any personal or family history of bipolar disorder, mania, or hypomania.

Discontinuation syndrome: Adverse reactions after discontinuation of serotonergic antidepressants, particularly after abrupt discontinuation, include: nausea, sweating, dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), tremor, anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible.

Others: seizures, closed angle glaucoma, hyponatremia.

SPECIAL POPULATIONS:

Dosage for hepatically impaired patients: The use of Sertraline in patients with liver disease should be approached with caution. The effects of Sertraline in patients with moderate and severe hepatic impairment have not been studied. If Sertraline is administered to patients with liver impairment, a lower or less frequent dose should be used.

Treatment of pregnant women during the third trimester: Neonates exposed to SERTRALINE and other SSRIs or SNRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. When treating pregnant women with SERTRALINE during the third trimester, the physician should carefully consider the potential risks and benefits of treatment. The physician may consider tapering Sertraline in the third trimester.

Geriatric use: No overall differences in the pattern of adverse reactions were observed in the geriatric clinical trial subjects relative to those reported in younger subjects, and other reported experience has not identified differences in safety patterns between the elderly and younger subjects. As with all medications, greater sensitivity of some older individuals cannot be ruled out. The overall profile of adverse events was generally similar. Urinary tract infection was the only adverse event not appearing and reported at an incidence of at least 2% and at a rate greater than placebo in placebo-controlled trials. SSRIS and SNRIs, including SERTRALINE have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event.

CONTRAINDICATIONS:

SERTRALINE is contraindicated in patients:

- Taking, or within 14 days of stopping, MAOIs, (including the MAOIs linezolid and intravenous methylene blue) because of an increased risk of serotonin syndrome.
- Taking pimozide.
- With known hypersensitivity to Sertraline (e.g., anaphylaxis, angioedema).

DRUG INTERACTIONS:

Sertraline can have clinically significant drug interactions with MAO inhibitors (selegiline, tranylcypromine, isocarboxazid, phenelzine, linezolid, methylene blue), pimozide, serotonergic drugs (SNRIs, triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's Wort), apirin, heparin, warfarin and clopidogrel, phenytoin and drugs metabolized by CYP2D6 including propafenone, flecainide, atomoxetine, desipramine, dextromethorphan, metoprolol, nebivolol, perphenazine, thoridazine, tolterodine, venlafaxine.

ADVERSE REACTIONS:

Most common adverse reactions (>5% and twice placebo) in pooled placebo controlled MDD, OCD, PD, PTSD, SAD and PMDD clinical trials were nausea, diarrhea/loose stool, tremor, dyspepsia, decreased appetite, hyperhidrosis, ejaculation failure, and decreased libido.

The following adverse reactions are reported frequently:

- Hypersensitivity reactions to Sertraline
- QT prolongation and ventricular arrhythmias when taken with pimozide
- Suicidal thoughts and behaviors
- Serotonin syndrome
- Increased risk of bleeding
- Activation of mania/hypomania
- Discontinuation syndrome
- Seizures
- Angle-closure glaucoma
- Hyponatremia

General: Frequent: back pain, asthenia, malaise, weight increase; **Infrequent:** fever, rigors, generalized edema; **Rare:** face edema, aphthous stomatitis.

Male and female sexual dysfunction: Although changes in sexual desire, sexual performance and sexual satisfaction often occur as manifestations of a

psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that selective serotonin reuptake inhibitors (SSRIs) can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance and satisfaction are 33 difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling, are likely to underestimate their actual incidence. There are no adequate and well-controlled studies examining sexual dysfunction with Sertraline treatment. Priapism has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects.

Other adverse events in pediatric patients: In over 600 pediatric patients treated with SERTRALINE the overall profile of adverse events was generally similar to that seen in adult studies. However, the following adverse events, from controlled trials were reported at an incidence of at least 2% and occurred at a rate of at least twice the placebo rate (N=281 patients treated with SERTRALINE: fever, hyperkinesia, urinary incontinence, aggressive reaction, sinusitis, epistaxis and purpura.

Post marketing experience: The following adverse reactions have been identified during post approval use of Sertraline. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Bleeding or clotting disorders - increased coagulation times (altered platelet function) Cardiac disorders – AV block, bradycardia, atrial arrhythmias, QT-interval prolongation, ventricular tachycardia (including Torsade de Pointes)
- Endocrine disorders - gynecomastia, hyperprolactinemia, menstrual irregularities, SIADH Eye disorders - blindness, optic neuritis, cataract Hepatobiliary disorders – severe liver events (including hepatitis, jaundice, liver failure with some fatal outcomes), pancreatitis Hemic and Lymphatic – agranulocytosis, aplastic anemia and pancytopenia, leukopenia, thrombocytopenia, lupus-like syndrome, serum sickness Immune system disorders – angioedema.
- Metabolism and nutrition disorders – hyponatremia, hyperglycemia
- Nervous system disorders - serotonin syndrome, extrapyramidal symptoms (including akathisia and dystonia), oculogyric crisis Psychiatric disorders – psychosis, enuresis, paroniria
- Renal and urinary disorders - acute renal failure
- Respiratory, thoracic and mediastinal disorders - pulmonary hypertension
- Skin and subcutaneous tissue disorders - photosensitivity skin reaction and other severe cutaneous reactions, which potentially can be fatal, such as Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN)
- Vascular disorders - cerebrovascular spasm (including reversible cerebral vasoconstriction syndrome and Call-Fleming syndrome), vasculitis.

OVERDOSAGE:

The most common signs and symptoms associated with non-fatal Sertraline hydrochloride overdosage were somnolence, vomiting, tachycardia, nausea, dizziness, agitation and tremor. Other important adverse events reported with Sertraline hydrochloride overdose (single or multiple drugs) include bradycardia, bundle branch block, coma, convulsions, delirium, hallucinations, hypertension, hypotension, manic reaction, pancreatitis, QT-interval prolongation, serotonin syndrome, stupor and syncope.

Overdose management: Treatment should consist of general measures employed in the management of overdosage with any antidepressant. Ensure an adequate airway, oxygenation and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion, or in symptomatic patients. Activated charcoal should be administered. Due to large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion and exchange transfusion are unlikely to be of benefit. No specific antidotes for Sertraline are known. In managing overdosage, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center on the treatment of any overdose.

INSTRUCTIONS:

- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Sabert Tablet 50 mg	:	Pack of 3 x 10 tablets.
Sabert Tablet 100 mg	:	Pack of 2 x 10 tablets.

Manufactured by:
WnsFeild Pharmaceuticals.
Plot # 122, Block A, Phase V, Industrial Estate, Hattar, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

گرمی، دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

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