For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Inosert

Sertraline Tablets

DESCRIPTION

Sertraline is a selective serotonin reuptake inhibitor (SSRI) for oral administration. Sertraline hydrochloride has the following chemical name: (1S-cis) – 4 - (3,4 - dichlorophenyl) - 1,2,3,4 – tetrahydro –N-methyl-1-naphthalenamine hydrochloride. The empirical formula is $C_{17}H_{17}NCl_2HCl$ with molecular weight of 342.7 (free base 306.2).

COMPOSITION

Inosert-50

Each film-coated tablet contains:
Sertraline Hydrochloride
equivalent to Sertraline 50 mg

Inosert-100

Each film-coated tablet contains:
Sertraline Hydrochloride
equivalent to Sertraline 100mg

PRODUCT DESCRIPTION

Inosert-50: White to off white, caplet shaped, biconvex, film coated tablets.

Inosert-100: White to off white, caplet shaped, biconvex, film coated tablets.

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS

Sertraline inhibits the CNS neuronal uptake of serotonin (5HT). Sertraline also blocks the uptake of serotonin into human platelets. Sertraline is a potent and selective inhibitor of neuronal serotonin reuptake and has only very weak effects on norepinephrine and dopamine neuronal reuptake. Sertraline's inhibition of serotonin reuptake enhances serotonergic transmission, which results in subsequent inhibition of adrenergic activity in the locus ceruleus. Sertraline has no affinity for muscarinic, serotonergic, dopaminergic adrenergic, histaminergic, GABA or benzodiazepine receptors. It is devoid of stimulant, sedative or anticholinergic activity or cardiotoxicity in animals.

PHARMACOKINETICS

Sertraline appears to be slowly but well absorbed from the GI tract following oral administration with peak plasma concentrations occurring about 4.5 to 8.4 hours after ingestion. Area under the plasma concentration time curve (AUC) was slightly increased when drug was administered with food but the C_{max} was 25% greater, while the time to reach peak plasma concentration (T_{max}) decreased from 8 hours post-dosing to 5.5 hours. Sertraline is widely distributed throughout body tissues and is approximately 98% bound to plasma proteins. Sertraline undergoes extensive first pass metabolism. Theprincipal initial pathway of metabolism for sertraline is N-demethylation. Sertraline and N-desmethylsertraline are both extensively metabolized in man and the resultant metabolites are excreted in faeces and urine in equal amounts. The average terminal elimination half-life of plasma sertraline is about 26 hours.

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

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, PTSD and Social Phobia — Patients not responding to a 50 mg dose may benefit from dose increases. Dose changes should be made at intervals 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 the Elderly — The same dose range as in younger patients may be used in the elderly. Over 700 elderly patients (>65 years) have participated in clinical studies which demonstrated the efficacy of sertraline in this patient population. The pattern and incidence of adverse reactions in the elderly was 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 (see section- Warnings and Precautions for Use).

Use 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 (see section -Warnings and Precautions for Use).

CONTRAINDICATION

Sertraline is contraindicated in patients with a hypersensitivity to Sertraline or any of the inactive ingredients in the tablet.

Concomitant use in patients taking pimozide is contraindicated.

WARNINGS AND PRECAUTIONS

WARNINGS

Clinical worsening and suicide risk

Patients with major depressive disorder (MDD), 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.

Patients being treated with antidepressants for any indication should be 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. 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.

Screening patients for bipolar disorder

Prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that sertraline is not approved for use in treating bipolar depression.

Potential for interaction with monoamine oxidase inhibitors

Serious fatal reactions have occurred in patients receiving Sertraline in combination with a monoamine oxidase inhibitor (MAOI). These reactions can also occur in patients who have recently discontinued an SSRI and have been started on an MAOI. Sertraline should not be used in combination with an MAOI, or within14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping sertraline before starting an MAOI.

PRECAUTIONS

General

Activation of mania/hypomania - Hypomania or mania occurred in sertraline treated patients.

Weight Loss - Significant weight loss may be an undesirable result of treatment with sertraline for some patients, but rarely patients have discontinued the drug for weight loss. The drug should be used with caution in patients who may be adversely affected by these effects (e.g. underweight patients).

Seizure - Patients may experience seizures during treatment with sertraline. Hence, sertraline should be introduced with care in patients with a seizure disorder. Hence, Sertraline should be introduced with care in patients with a seizure disorder.

Discontinuation of treatment with sertraline – Adverse events have occurred upon discontinuation of sertraline and other SSRIs and SNRIs drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g. paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with sertraline. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the

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physician may continue decreasing the dose but at a more gradual rate.

Abnormal bleeding- Bleeding episodes have occurred in the treatment with psychotropic drugs that interfere with serotonin reuptake Patients should be cautioned regarding the risk of bleeding associated with the concomitant use of sertraline with non-selective NSA Ds (i.e., NSAIDs that inhibit both cyclooxygenase isoenzymes, COX 1 and 2), Aspirin, or other drugs that affect coagulation.

Weak uricosuric effect - Sertraline is associated with a mean decrease in serum uric acid.

Endocrine effects - Sertaline has been associated with hypothyroidism, elevated serum thyrotropin, and/or reduced serum thyroxine concentrations. It is recommended that thyroid function be reassessed periodically in patients with thyroid disease who are receiving sertraline.

Use in patients with concomitant illness - Caution is advisable in using sertralinein patients with diseases or conditions that could affect metabolism or hemodynamic responses.

Sertraline is not associated with the development of significant ECG abnormalities. The use of sertraline in patients with liver disease must be approached with caution. If sertraline is administered to patients with liver impairment, a lower or less frequent dose should be used. The effects of sertraline in patients with moderate to severe hepatic impairment have not been studied. Pharmacokinetics and protein binding of sertraline are unaffected by renal disease. There is no need for dosage adjustment in patients with renal impairment.

In patients with diabetes, treatment with an SSRI may alter glycaemic control, possibly due to improvement of depressive symptoms. Insulin and/or oral hypoglycaemic dosage may be needed to be adjusted.

Interference with cognitive & motor performance- Sertraline did not cause sedation & did not interfere with psychomotor performance.

Hyponatremia - Elderly individuals, some in patients taking diuretics or who were otherwise volume depleted may be at a greater risk of developing hyponatremia with SSRIs and SNRIs, including sertraline. Discontinuation of sertraline should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.

Platelet function - Abnormal bleeding or purpura has occurred in patients taking sertraline, however it is unclear whether sertraline had a causative role.

Effects on ability to drive and use machines – Clinical pharmacology studies have shown that sertraline has no effect on psychomotor performance. However, since antidepressant or antiobsessional drugs may impair the abilities required to perform potentially hazardous tasks such as driving a car or operating machinery, the patient should be cautioned accordingly. Sertraline should not be administered with benzodiazepines or other tranquilizers in patients who drive or operate machinery.

Usage in pregnancy and lactation

Sertraline should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. The effect of Sertraline on labor and delivery in humans is unknown.

Caution should be exercised when sertraline is administered to a nursing woman.

Usage in geriatrics

As with all medications, greater sensitivity of some older individuals cannot be ruled out. Sertraline has been associated with cases of clinically significant hyponatremia in elderly patients.

INTERACTIONS WITH OTHER MEDICAMENTS

- Because sertraline is tightly bound to plasma protein, the administration of sertraline to a patient taking another drug, which is tightly bound to protein (e.g., warfarin, digitoxin) may cause a shift in plasma concentrations potentially resulting in an adverse effect. Conversely, adverse effects may result from displacement of protein bound sertraline by other tightly bound drugs.
- Sertraline inhibits cytochrome P4502D6 activity and, thus, may increase the plasma concentrations of co-administered drugs that are metabolized by P4502D6 (e.g. tricyclic antidepressants, Type 1C antiarrhythmics).
- Prothrombin time should be carefully monitored when sertraline therapy is initiated or stopped in patients who have been given warfarin.
- Cimetidine increases concentration of sertraline.
- Sertraline decreases clearance of diazepam and tolbutamide.
- Sertraline does not increase plasma concentrations of terfenadine, carbamazepine and cisapride.
- Plasma lithium levels should be monitored following initiation of sertraline therapy with appropriate adjustments to the lithium dose.
- Sertraline increases AUC and Cmax of pimozide. Concomitant administration of sertraline and pimozide should be contraindicated.
- The concomitant use of sertraline and alcohol is not recommended.
- Caution is advised if the concomitant administration of sertraline and CNS active drugs are required.
- Concomitant use of sertraline with tryptophan should be undertaken with caution.
- Care and prudent medical judgement should be exercised when switching, particularly from long-acting agents to sertraline.
- If concomitant treatment with sumatriptan and sertraline is clinically warranted, appropriate observation of the patient (particularly regarding weakness, hyperreflexia and incoordination) is advised.
- Sertraline has no effect on serum digoxin levels whereas it causes decrease in antipyrine half-life due to microsomal enzyme induction.
- Clinicians should be aware of the potential for serotonin syndrome when isoniazid is given in combination with sertraline.
- Caution should be exercised if clozapine is used in patients receiving selective serotonin reuptake inhibitors and a reduction in clozapine dosage should be considered.
- Concurrent use of a non-selective NSAID (i.e., NSAIDs that inhibit both cyclooxygenase isoenzymes, COX 1 and 2) or aspirin potentiated the risk of bleeding. Thus, patients should be cautioned about the use ofsuch drugs concurrently with sertraline.
- There are no clinical studies establishing the risks or benefits of the combined use of electroconvulsive therapy (ECT) and sertraline.

Pregnancy & Lactation

Sertraline should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. The effect of Sertraline on labor and delivery in humans is unknown.

Caution should be exercised when sertraline is administered to a nursing woman.

SIDE EFFECTS

The adverse events associated with the use of sertraline for the treatment of adult patients with major depressive disorder, OCD, panic disorder, PTSD, PMDD and social anxiety disorder are:

Autonomic nervous system disorders - Ejaculation Failure, dry mouth, increased sweating

Central & peripheral nervous system disorders – Somnolence, tremor, dizziness, headache, paresthesia

General - Fatigue, pain, malaise

Gastrointestinal disorders - Abdominal pain, anorexia, constipation, diarrhea/loose stools, dyspepsia, nausea, vomiting

Psychiatric disorders - Agitation, anxiety, insomnia, decreased libido, nervousness

Disorders of skin – Rash

Special senses - Abnormal vision

Male and female sexual dysfunction with SSRIs

Sexual side effects include ejaculation failure (primarily delayed ejaculation) and decreased libido. 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.

DRUG ABUSE AND DEPENDENCE

Physical and psychological dependence - Sertraline did not produce the positive subjective effects indicative of abuse potential, such as euphoria or drug liking. Sertraline does not have any tendency for a withdrawal syndrome or any drug-seeking behavior. Physicians should carefully evaluate patients for history of drug abuse and follow such patients closely, observing them for signs of sertraline misuse or abuse (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

SYMPTOMS AND TREATMENT OF OVERDOSE

The most common signs and symptoms associated with non-fatal sertraline 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.

Overdosage management includes general measures such as ensure an adequate airway, oxygenation and ventilation, monitor cardiac rhythm and vital signs, general supportive and symptomatic measures. Gastric lavage with a large-bore orogastric tube with appropriate airway protection may be indicated if performed soon after ingestion, or in symptomatic patients. Activated charcoal should be administered. 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.

STORAGE

Store below 30°C in a dry place, away from light
KEEP OUT OF REACH OF CHILDREN

PRESENTATION

Blister strip of 14 tablets (Box of 28's)

DATE OF REVISION

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Made in India by
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