SUMMARY OF PRODUCT CHARACTERISTICS

NAME OF DRUG PRODUCT: Sertraline Tablets 50 mg.
Sertraline Tablets 100 mg.

(TRADE) NAME OF PRODUCT: AURASERT 50.
AURASERT 100.

STRENGTH: 50 mg and 100 mg.

PHARMACEUTICAL DOSAGE FORM: Tablet.

QUALITATIVE AND QUANTITATIVE COMPOSITIONS:

Sertraline Tablets 50 mg

Each film-coated tablet contains:

Sertraline Hydrochloride equivalent to Sertraline 50 mg.

Sertraline Tablets 100 mg

Each film-coated tablet contains:

Sertraline Hydrochloride equivalent to Sertraline 100 mg.

PHARMACEUTICAL FORM:

Sertraline Tablets 50 mg: White coloured, biconvex, capsule shaped, film coated tablets debossed with 'A' on one side and with a score line in between '8' and '1' on the other side.

Sertraline Tablets 100 mg: White coloured, biconvex, capsule shaped, film coated tablets debossed with 'A' on one side and '82' on the other side.

CLINICAL PARTICULARS:

Therapeutic indications

Sertraline is indicated for the treatment of symptoms of depressive illness, including accompanying symptoms of anxiety. Following satisfactory response, continuation with Sertraline therapy is effective in preventing relapse of the initial episode of depression or recurrence of further depressive episodes, including accompanying symptoms of anxiety.

Sertraline is also indicated for the treatment of obsessive compulsive disorder (OCD). Following initial response, Sertraline has been associated with sustained efficacy, safety and tolerability in up to two years treatment of OCD.

Sertraline is also indicated for the treatment of paediatric patients with OCD.

Treatment with Sertraline cannot normally recommended for male patients with PTSD. Treatment should subsequently be withdrawn unless there is clear evidence of therapeutic benefit.

Sertraline is not indicated for use in children and adolescents under the age of 18 years with major depressive disorder.

Posology and method of administration

Sertraline should be given as a single daily dose. Sertraline tablets can be administered with or without food.

Adults

Depression (including accompanying symptoms of anxiety): The starting dose is 50 mg daily and the usual antidepressant dose is 50 mg daily. In some patients, doses higher than 50 mg may be required.

Obsessive Compulsive Disorder: The starting dose is 50 mg daily, and the therapeutic dose range is 50-200 mg daily.

Post-Traumatic Stress Disorder: Treatment for PTSD should be initiated at 25 mg/day. After one week, the dose should be increased to 50 mg once daily. PTSD is a heterogeneous illness and some patient groups fulfilling the criteria for PTSD do not appear to be responsive to treatment with Sertraline. Dosing should be reviewed periodically by the prescribing physician to determine response to therapy and treatment should be withdrawn if there is no clear evidence of efficacy.

Depression *(including accompanying symptoms of anxiety)*, OCD and PTSD: In some patients doses higher than 50 mg daily may be required. In patients with incomplete response but good toleration at lower doses, dosage adjustments should be made in 50 mg increments over a period of weeks to a maximum of 200 mg daily.

Once optimal therapeutic response is achieved the dose should be reduced, depending on therapeutic response, to the lowest effective level. Dosage during prolonged maintenance therapy should be kept at the lowest effective level, with subsequent adjustments

depending on therapeutic response. The onset of therapeutic effect may be seen within 7 days, although 2-4 weeks (and even longer in OCD) are usually necessary for full activity. A longer treatment period, even beyond 12 weeks in some cases, may be required in the case of a therapeutic trial in PTSD.

Use in children aged 6-17 years: Treatment should only be initiated by specialists. The safety and efficacy of Sertraline has been established in paediatric OCD patients (aged 6-17). The administration of Sertraline to paediatric OCD patients (aged 13-17) should commence at 50 mg/day. Therapy for paediatric OCD patients (aged 6-12) should commence at 25 mg/day increasing to 50 mg/day after 1 week. Subsequent doses may be increased in case of lack of response in 50 mg/day increments up to 200 mg/day as needed. However, the generally lower body weights of children compared to adults should be taken into consideration in advancing the dose from 50 mg, in order to avoid excessive dosing. Given the 24 hour elimination half-life of Sertraline, dose changes should not occur at intervals of less than 1 week.

Children aged less than six years Sertraline is not recommended in children under six years of age.

Use in the elderly No special precautions are required. The usual adult dose is recommended. The pattern and incidence of adverse reactions in the elderly is similar to that in younger patients.

Sertraline tablets are for oral administration only.

Contraindications

Sertraline is contraindicated in patients with a known hypersensitivity to sertraline.

Monoamine oxidase inhibitors: Serious and sometimes fatal reactions occurs in patients receiving an SSRI in combination with a monoamine oxidase inhibitor (MAOI), including the selective MAOI selegiline and the reversible MAOI (RIMA) moclobemide.

Symptoms of a drug interaction with 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.

Sertraline should not be used in combination with a MAOI. Sertraline may be started 14 days after discontinuing treatment with an irreversible MAOI and at least one day after

discontinuing treatment with the reversible MAOI (RIMA), moclobemide. At least 14 days should elapse after discontinuing Sertraline treatment before starting a MAOI or RIMA.

Use in hepatic impairment: Sertraline should not be used in patients with significant hepatic dysfunction.

Concomitant use in patients taking pimozide is contra-indicated.

Sertraline should not be used in children and adolescents under the age of 18 years with Major depressive disorder.

Special warnings and precautions for use

Use in patients with renal or hepatic impairment: As with many other medications, Sertraline should be used with caution in patients with renal and hepatic impairment.

Since sertraline is extensively metabolised, excretion of unchanged drug in urine is a minor route of elimination. In patients with mild to moderate renal impairment (creatinine clearance 20-50 ml/min) or severe renal impairment (creatinine clearance <20 ml/min), single dose pharmacokinetic parameters were not significantly different compared with controls. However, caution is advised when treating patients with renal impairment.

Sertraline is extensively metabolised by the liver. 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.

Diabetes: 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.

Seizures: are a potential risk with antidepressant or antiobsessional drugs. The drug should be discontinued in any patient who develops seizures. Sertraline should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. Sertraline should be discontinued if there is an increase in seizure frequency.

Electroconvulsive therapy (ECT): Concurrent admini-stration of Sertraline and ECT, caution is advisable.

Mania: Sertraline should be used with caution in patients with a history of mania/hypomania. Sertraline should be discontinued in any patient entering a manic phase.

Suicide: As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored during this period. The possibility of a suicide attempt is inherent in depression and may persist until significant therapeutic effect is achieved and it is general clinical experience with all antidepressant therapies that the risk of suicide may increase in the early stages of recovery.

Haemorrhage: This includes cutaneous bleeding abnormalities such as ecchymoses and purpura with SSRIs.

Caution is advised in patients taking SSRIs, particularly in concomitant use with drugs known to affect platelet function (e.g. atypical antipsychotics and phenothiazines, most tricyclic antidepressants, aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) as well as in patients with a history of bleeding disorders.

Use in the elderly: The pattern and incidence of adverse reactions in the elderly is similar to that in younger patients.

Interaction with other medicinal products and other forms of interaction

Centrally active medication: Caution is advised if Sertraline is administered with other centrally active medication. In particular, SSRIs have the potential to interact with tricyclic antidepressants leading to an increase in plasma levels of the tricyclic antidepressant. A possible mechanism for this interaction is the inhibitory effect of SSRIs on the CYP2D6 isoenzyme. There is variability among the SSRIs in the extent to which they inhibit the activity of CYP2D6.

The clinical significance of this depends on the extent of inhibition and the therapeutic index of the co-administered drug.

Pimozide–Due to the narrow therapeutic index of pimozide, concomitant use of pimozide and Sertraline is contraindicated.

Alcohol: The concomitant use of Sertraline and alcohol in depressed patients is not recommended.

Lithium and Tryptophan: The co-administration of Sertraline and lithium did not significantly alter lithium pharmacokinetics.

Co-administration of Sertraline with lithium results in an increase in tremor relative to placebo, indicating a possible pharmacodynamic interaction. Enhanced effects occur when SSRIs is given with lithium or tryptophan and therefore the concomitant use of SSRIs with these drugs should be undertaken with caution.

Serotonergic drugs: Care and prudent medical judgement should be exercised when switching, particularly from long-acting agents.

Serotonergic drugs, such as tramadol, sumatriptan or fenfluramine, should not be used concomitantly with Sertraline, due to a possible enhancement of 5-HT associated effects.

St. John's Wort: Concomitant use of the herbal remedy St. John's wort (Hypericum perforatum) in patients receiving SSRIs should be avoided since there is a possibility of serotonergic potentiation.

Other drug interactions: Since Sertraline is bound to plasma proteins, the potential of Sertraline to interact with other plasma protein bound drugs should be borne in mind.

Co-administration of Sertraline (200 mg daily) with diazepam or tolbutamide resulted in small, statistically significant changes in some pharmacokinetic parameters. Co-administration with cimetidine causes a substantial decrease in sertraline clearance. Sertraline had no effect on the beta-adrenergic blocking ability of atenolol.

Co-administration of Sertraline (200 mg daily) with warfarin results in slight increase in prothrombin time, Accordingly, prothrombin time should be carefully monitored when Sertraline therapy is initiated or stopped.

Sertraline (200 mg daily), do not potentiate the effects of carbamazepine, haloperidol or phenytoin on cognitive and psychomotor performance.

Pregnancy and lactation

Pregnancy: As with all drugs Sertraline should only be used in pregnancy if the potential benefits of treatment to the mother outweigh the possible risks to the developing foetus.

Lactation: Sertraline excretes in breast milk, if treatment with Sertraline is considered necessary, discontinuation of breast feeding should be considered.

Effects on ability to drive and use machines

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 benzodiaze-pines or other tranquillizers in patients who drive or operate machinery.

Undesirable effects

Side effects include nausea, diarrhoea/loose stools, anorexia, dyspepsia, tremor, dizziness, insomnia, somnolence, increased sweating, dry mouth and sexual dysfunction (principally ejaculatory delay in males).

In paediatric OCD patients, side effects, which include significantly more frequently with sertraline than placebo are: headache, insomnia, agitation, anorexia, tremor. Most are of mild to moderate severity.

Cardiovascular: Blood pressure disturbances including postural hypotension, tachycardia.

Eye disorders: Abnormal vision.

Gastro-intestinal: Vomiting, abdominal pain.

Nervous system: Amnesia, headache, drowsiness, movement disorders, paraesthesia, hypoaesthesia, depressive symptoms, hallucinations, aggressive reaction, agitation, anxiety, psychosis, depersonali-sation, nervousness, panic reaction and signs and symptoms associated with serotonin syndrome which include fever, rigidity, confusion, agitation, diaphoresis, tachycardia, hypertension and diarrhoea.

Convulsions (Seizures): Sertraline should be discon-tinued in any patient who develops seizures.

Musculoskeletal: Arthralgia, myalgia.

Hepatic/pancreatic: Rarely, pancreatitis and serious liver events (including hepatitis, jaundice and liver failure). Asymptomatic elevations in serum transaminases (SGOT and SGPT) occur in association with sertraline administration (0.8 – 1.3%), with an increased risk associated with the 200 mg daily dose. The abnormalities usually occurred within the first 1 to 9 weeks of drug treatment and promptly diminished upon drug discontinuation.

Renal & urinary disorders: Urinary retention.

Reproductive: Hyperprolactinemia, galactorrhoea, menstrual irregularities, anorgasmy.

Skin and allergic reactions: Rash (including erythema multiforme, photosensitivity), angioedema, ecchymoses, pruritus and anaphylactoid reactions.

Metabolic Rarely occurs hyponatremia and appeared to be reversible when sertraline was discontinued. Some cases were possibly due to the syndrome of inappropriate antidiuretic hormone secretion. The majority of reports were associated with older patients and patients taking diuretics or other medications.

Haematologic: Patients taking sertraline rarely shows altered platelet function. Also thrombocytopenia, abnormal bleeding or purpura may seen in several patients taking sertraline.

General: Malaise.

Other: Withdrawal reactions occur with Sertraline. Common symptoms include dizziness, paraesthesia, headache, anxiety and nausea. Abrupt discontinuation of treatment with Sertraline should be avoided. The majority are experienced on withdrawal of Sertraline are non-serious and self-limiting.

Overdosage

Sertraline has a wide margin of safety in overdose. Deaths involving overdoses of Sertraline in combination with other drugs and/or alcohol occurs. Therefore, any overdosage should be treated aggressively.

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

No specific therapy is recommended and there are no specific antidotes to Sertraline. Establish and maintain an airway, ensure adequate oxygenation and ventilation. Activated charcoal, which may be used with sorbitol, may be as or more effective than emesis or lavage and should be considered in treating overdose. Cardiac and vital signs monitoring is recommended along with general symptomatic and supportive measures. Due to the large volume of distribution of sertraline, forced diuresis, dialysis, haemoperfusion and exchange transfusion are unlikely to be of benefit.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Sertraline is a potent and specific inhibitor of neuronal serotonin (5-HT) uptake in vitro and in vivo, but is without affinity for muscarinic, serotonergic, dopaminergic, adrenergic, histaminergic, GABA or benzodiazepine receptors.

Unlike tricyclic antidepressants, no weight gain is observed with treatment for depression.

Sertraline do not produce physical or psychological dependence.

Pharmacokinetic properties

Sertraline exhibits dose proportional pharmacokinetics over a range of 50-200 mg. After oral administration of sertraline in man, peak blood levels occur at about 4.5 - 8.4 hours. Daily doses of sertraline achieve steady state after one week. Sertraline has a plasma half-life of approximately 26 hours with a mean half-life for young and elderly adults ranging from 22-36 hours. Sertraline is approximately 98% bound to plasma proteins. The principal metabolite, N-desmethylsertraline, is inactive in in vivo models of depression and has a half-life of approximately 62-104 hours. Sertraline and N-desmethylsertraline are both extensively metabolised in man and the resultant metabolites excreted in faeces and urine in equal amounts. Only a small amount (<0.2%) of unchanged sertraline is excreted in the urine.

The pharmacokinetics of sertraline in paediatric OCD patients has been shown to be comparable with adults (although paediatric patients metabolise sertraline with slightly greater efficiency). However, lower doses may be advisable for paediatric patients given their lower body weights (especially 6-12 years), in order to avoid excessive plasma levels.

The pharmacokinetics of sertraline in elderly patients is similar to younger adults.

Food does not significantly change the bioavailability of Sertraline tablets.

PHARMACEUTICAL PARTICULARS

List of excipients

Microcrystalline cellulose, Sodium Starch Glycolate, Hydroxypropylcellulose, Calcium hydrogen Phosphate Dihydrate, Magnesium Stearate, Opadry White and Purified Water.

Incompatibilities

None.

Shelf life

36 months.

Special precautions for storage

Store at or below 30°C.

Marketing authorisation holder

Aurobindo Pharma Limited

Marketing authorisation number(s)

06045/6175/NMR/2018

Date of first authorisation/renewal of the authorization

Jun 8, 2021

Date of revision of the text

Jun 8, 2021