Restraline®

Sertraline hydrochloride

FORMS AND PRESENTATION

Restraline®: Film Coated Tablets. Box of 30.

COMPOSITION

Restraline®: Each film coated tablet contains Sertraline hydrochloride equivalent to Sertraline 50mg.

Excipients: microcrystalline cellulose, povidone, sodium starch glycolate, dibasic calcium phosphate dihydrate, magnesium stearate, FD&C Blue No.2, hydroxypropyl methylcellulose, polyethylene glycol, polysorbate 80, titanium dioxide.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Selective serotonin reuptake inhibitors (SSRI), ATC code: N06AB06.

Mechanism of action

Sertraline is a potent and specific inhibitor of neuronal serotonin (5 HT) uptake in vitro, which results in the potentiation of the effects of 5-HT in animals. It has only very weak effects on norepinephrine and dopamine neuronal reuptake. At clinical doses, sertraline blocks the uptake of serotonin into human platelets. In accord with its selective inhibition of 5-HT uptake, sertraline does not enhance catecholaminergic activity. Sertraline has no affinity for muscarinic (cholinergic), serotonergic, dopaminergic, adrenergic, histaminergic, GABA or benzodiazepine receptors. The chronic administration of sertraline in animals was associated with down-regulation of brain norepinephrine receptors as observed with other clinically effective antidepressants and antiobsessional drugs.

Pharmacokinetic properties

Absorption

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

Distribution

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

Biotransformation

Sertraline undergoes extensive first-pass hepatic metabolism. Based on clinical and *in-vitro* data, it can be concluded that sertraline is metabolized by multiple pathways including CYP3A4, CYP2C19 and CYP2B6. Sertraline and its major metabolite desmethylsertraline are also substrate of P Glycoprotein *in-vitro*.

Elimination

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

Pharmacokinetics in specific patient groups

Liver function impairment: In patients with liver damage, the half-life of sertraline is prolonged and AUC is increased three-fold.

INDICATIONS

Restraline® is indicated for the treatment of:

- Major depressive episodes. Prevention of recurrence of major depressive episodes.
- Panic disorder, with or without agoraphobia.
- Obsessive compulsive disorder (OCD) in adults and paediatric patients aged 6-17 years.
- Social anxiety disorder.
- Post traumatic stress disorder (PTSD).

CONTRAINDICATIONS

– Hypersensitivity to the active substance or any of the excipients listed.
– Concomitant treatment with irreversible monoamine oxidase inhibitors (MAOIs) is contraindicated due to the risk of serotonin syndrome with symptoms such as agitation, tremor and hyperthermia.
– Concomitant intake of pimozide is contraindicated.

PRECAUTIONS

Serotonin Syndrome (SS) or Neuroleptic Malignant Syndrome (NMS): The risk of SS or NMS with Selective Serotonin Reuptake Inhibitors (SSRIs) is increased with concomitant use of other serotonergic drugs (including other serotonergic antidepressants, triptans), with drugs which impair metabolism of serotonin (including MAOIs e.g. methylene blue), antipsychotics and other dopamine antagonists, and with opiate drugs. Patients should be monitored for the emergence of signs and symptoms of SS or NMS syndrome. Concomitant administration of sertraline and buprenorphine/opioids may result in SS, a potentially life-threatening condition. If concomitant treatment with other serotonergic agents is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Symptoms of SS may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms. If SS is suspected, a dose reduction or discontinuation of therapy should be considered depending on the severity of the symptoms.

Switching from (SSRIs), antidepressants or antiobsessional drugs: Care and prudent medical judgment should be exercised when switching, particularly from long-acting agents such as fluoxetine.

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

QTc Prolongation: Sertraline should be used with caution in patients with additional risk factors for QTc prolongation such as cardiac disease, hypokalaemia or hypomagnesemia, familial history of QTc prolongation, bradycardia and concomitant use of medications which prolong QTc interval.

Activation of hypomania or mania: Sertraline should be used with caution in patients with a history of mania/hypomania. Close surveillance by the physician is required. Sertraline should be discontinued in any patient entering a manic phase.

Schizophrenia: Psychotic symptoms might become aggravated in schizophrenic patients.

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

Suicide/suicidal thoughts/suicide attempts or clinical worsening: Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment should receive careful monitoring during treatment. Close supervision of patients and in particular those at high risk should accompany drug therapy especially in early treatment and following dose changes.

Sexual dysfunction: SSRIs may cause symptoms of sexual dysfunction. There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs.

Paediatric population: Sertraline should not be used in the treatment of children and adolescents under the age of 18 years, except for patients with OCD aged 6-17 years old.

Abnormal bleeding/Haemorrhage: SSRIs/SNRIs may increase the risk of postpartum haemorrhage. Caution is advised in patients taking SSRIs, particularly in concomitant use with drugs known to affect platelet function (e.g. anticoagulants, atypical antipsychotics and phenothiazines, most tricyclic antidepressants, acetylsalicylic acid and non-steroidal anti-inflammatory drugs (NSAIDs)) as well as in patients with a history of bleeding disorders.

Hyponatraemia: Hyponatraemia may occur as a result of treatment with SSRIs or SNRIs including sertraline. In many cases, hyponatraemia appears to be the result of a syndrome of inappropriate antidiuretic hormone secretion (SIADH). Cases of serum sodium levels lower than 110 mmol/l have been reported. Elderly patients may be at greater risk of developing hyponatraemia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume-depleted may be at greater risk. Discontinuation of sertraline should be considered in patients with symptomatic hyponatraemia and appropriate medical intervention should be instituted.

Withdrawal symptoms seen on discontinuation of sertraline treatment: Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt. The risk of withdrawal symptoms may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction. Dizziness, sensory disturbances (including paraesthesia), sleep disturbances (including insomnia and intense dreams), agitation or anxiety, nausea and/or vomiting, tremor and headache are the most commonly reported reactions. Generally, these symptoms are mild to moderate; however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment. Generally, these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that sertraline should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient's needs.

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

Hepatic impairment: The use of sertraline in patients with hepatic disease must be approached with caution. If sertraline is administered to patients with hepatic impairment, a lower or less frequent dose should be considered. Sertraline should not be used in patients with severe hepatic impairment.

Diabetes: In patients with diabetes, treatment with an SSRI may alter glycaemic control. Insulin and/or oral hypoglycaemic dosage may need to be adjusted.

Grapefruit juice: The administration of sertraline with grapefruit juice is not recommended.

Interference with urine screening tests: False-positive urine immunoassay screening tests for benzodiazepines have been reported in patients taking sertraline. This is due to lack of specificity of the screening tests. False-positive test results may be expected for several days following discontinuation of sertraline therapy. Confirmatory tests, such as gas chromatography/mass spectrometry, will distinguish sertraline from benzodiazepines.

Angle-Closure Glaucoma: SSRIs including sertraline may have an effect on pupil size resulting in mydriasis. This mydriatic effect has the potential to narrow the eye angle resulting in increased intraocular pressure and angle-closure glaucoma, especially in patients pre-disposed. Sertraline should therefore be used with caution in patients with angle-closure glaucoma or history of glaucoma.

Effects on ability to drive and use machines

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

LACTATION AND FERTILITY

Pregnancy

Use of sertraline during pregnancy has been reported to cause symptoms, compatible with withdrawal reactions, in some neonates, whose mothers had been on sertraline. This phenomenon has also been observed with other SSRI antidepressants. Sertraline is not recommended in pregnancy, unless the clinical condition of the woman is such that the benefit of the treatment is expected to outweigh the potential risk. Neonates should be observed if maternal use of sertraline continues into the later stages of pregnancy, particularly the third trimester. The following symptoms may occur in the neonate after maternal sertraline use in later stages of pregnancy: respiratory distress, cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycaemia, hypertonia, hypotonia, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying, somnolence and difficulty in sleeping. These symptoms could be due to either serotonergic effects or withdrawal symptoms. In a majority of instances, the complications begin immediately or soon (<24 hours) after delivery.

Epidemiological data have suggested that the use of SSRIs in pregnancy, particular in late pregnancy, may increase the risk of persistent pulmonary hypertension in the newborn (PPHN).

Breast-feeding

Published data concerning sertraline levels in breast milk show that small quantities of sertraline and its metabolite N-desmethylsertraline are excreted in milk. Generally negligible to undetectable levels were found in infant serum, with one exception of an infant with serum levels about 50% of the maternal level (but without a noticeable health effect in this infant). To date, no adverse effects on the health of infants nursed by mothers using sertraline have been reported, but a risk cannot be excluded. Use in nursing mothers is not recommended unless, in the judgment of the physician, the benefit outweighs the risk.

Fertility

Human case reports with some SSRI's have shown that an effect on sperm quality is reversible.

Impact on human fertility has not been observed so far.

DRUG INTERACTIONS

Contraindicated

Monoamine Oxidase Inhibitors

Irreversible MAOIs (e.g. selegiline): Restraline® must not be used in combination with irreversible MAOIs such as selegiline. Restraline® must not be initiated for at least 14 days after discontinuation of treatment with an irreversible MAOI. Restraline® must be discontinued for at least 7 days before starting treatment with an irreversible MAOI.

Reversible, selective MAO-A inhibitor (moclobemide): Due to the risk of serotonin syndrome, the combination of sertraline with a reversible and selective MAOI, such as moclobemide, should not be given. Following treatment with a reversible MAO-inhibitor, a shorter withdrawal period than 14 days may be used before initiation of Restraline® treatment. It is recommended that Restraline® should be discontinued for at least 7 days before starting treatment with a reversible MAOI.

Reversible, non-selective MAOI (linezolid): The antibiotic linezolid is a weak reversible and non-selective MAOI and should not be given to patients treated with sertraline.

Severe adverse reactions have been reported in patients who have recently been discontinued from an MAOI (e.g. methylene blue) and started on sertraline, or have recently had sertraline therapy discontinued prior to initiation of an MAOI. These reactions have included tremor, myoclonus, diaphoresis, nausea, vomiting, flushing, dizziness, and hyperthermia with features resembling neuroleptic malignant syndrome, seizures, and death.

Pimozide

While the mechanism of this interaction is unknown, due to the narrow therapeutic index of pimozide, concomitant administration of sertraline and

pimozide is contraindicated.
Co-administration with sertraline is not recommended
Sertraline should be used cautiously when co-administered with:
Buprenorphine/opioids as the risk of serotonin syndrome, a potentially life-threatening condition, is increased.
CNS depressants and alcohol
The co-administration of sertraline with a dose of 200 mg daily did not potentiate the effects of alcohol, carbamazepine, haloperidol, or phenytoin on cognitive and psychomotor performance in healthy subjects; however, the concomitant use of sertraline and alcohol is not recommended.
Other serotonergic drugs
Caution is also advised with fentanyl (used in general anaesthesia or in the treatment of chronic pain), other serotonergic drugs (including other serotonergic antidepressants, triptans), and with other opiate drugs.
Special Precautions
Drugs that Prolong the QT Interval
The risk of QTc prolongation and/or ventricular arrhythmias (e.g. TdP) may be increased with concomitant use of other drugs which prolong the QTc interval (e.g. some antipsychotics and antibiotics).
Lithium
In a placebo-controlled trial in normal volunteers, the co-administration of sertraline with lithium did not significantly alter lithium pharmacokinetics, but did result in an increase in tremor relative to placebo, indicating a possible pharmacodynamic interaction. When co-administering sertraline with lithium, patients should be appropriately monitored.
Phenytoin
As some case reports have emerged of high phenytoin exposure in patients using sertraline, it is recommended that plasma phenytoin concentrations be monitored following initiation of sertraline therapy, with appropriate adjustments to the phenytoin dose. In addition, co-administration of phenytoin may cause a reduction of sertraline plasma levels. It cannot be excluded that other CYP3A4 inducers, e.g. phenobarbital, carbamazepine, St John´s Wort, rifampicin may cause a reduction of sertraline plasma levels.
Triptans
There have been rare post-marketing reports describing patients with weakness, hyperreflexia, incoordination, confusion, anxiety and agitation following the use of sertraline and sumatriptan. Symptoms of serotonergic syndrome may also occur with other products of the same class (triptans). If concomitant treatment with sertraline and triptans is clinically warranted, appropriate observation of the patient is advised.
Warfarin
Co-administration of sertraline with a dose of 200 mg daily with warfarin resulted in a small but statistically significant increase in prothrombin time, which may in some rare cases unbalance the INR value. Accordingly, prothrombin time should be carefully monitored when sertraline therapy is initiated or stopped.
Cimetidine
Co-administration with cimetidine caused a substantial decrease in sertraline clearance.
Drugs affecting platelet function
The risk of bleeding may be increased when medicines acting on platelet function (e.g. NSAIDs, acetylsalicylic acid and ticlopidine) or other medicines that might increase bleeding risk are concomitantly administered with SSRIs, including sertraline.
Neuromuscular Blockers
SSRIs may reduce plasma cholinesterase activity resulting in a prolongation of the neuromuscular blocking action of mivacurium or other neuromuscular blockers.
Drugs Metabolized by Cytochrome P450
Sertraline may act as a mild-moderate inhibitor of CYP 2D6. Chronic dosing with sertraline 50mg daily showed moderate elevation (mean 23%-37%) of steady-state desipramine plasma levels (a marker of CYP 2D6 isozyme activity). Clinical relevant interactions may occur with other CYP 2D6 substrates with a narrow therapeutic index like class 1C antiarrhythmics such as propafenone and flecainide, TCAs and typical antipsychotics, especially at higher sertraline dose levels.
Sertraline does not act as an inhibitor of CYP 3A4, CYP 2C9, CYP 2C19, and CYP 1A2 to a clinically significant degree.
The intake of potent CYP3A4 inhibitors should be avoided during treatment with sertraline.
Sertraline plasma levels are enhanced by about 50% in poor metabolizers of CYP2C19 compared to rapid metabolizers. Interaction with strong inhibitors of CYP2C19, e.g. omeprazole, lansoprazole, pantoprazole, rabeprazole, fluoxetine, fluvoxamine cannot be excluded.

ADVERSE EFFECTS
Adverse effects are listed below by system organ class and frequency. Frequencies are defined as: very common (> 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1000 to < 1/100); rare (≥ 1/10000 to < 1/1000); not known (cannot be estimated from the available data).
Infections and infestations: upper respiratory tract infection, rhinitis, pharyngitis (common); gastroenteritis, otitis media (uncommon); diverticulitis (rare).
Neoplasms benign, malignant (including cysts and polyps): neoplasm (uncommon).
Blood and lymphatic system disorders: lymphadenopathy, thrombocytopenia, leukopenia (rare).
Immune system disorders: hypersensitivity, seasonal allergy (uncommon); anaphylactoid reaction (rare).
Endocrine disorders: hypothyroidism (uncommon); hyperprolactinaemia, inappropriate antidiuretic hormone secretion (rare).
Metabolism and nutrition disorders: decreased appetite, increased appetite (common); hypercholesterolaemia, diabetes mellitus, hypoglycaemia, hyperglycaemia, hyponatraemia (rare).
Psychiatric disorders: insomnia (very common); anxiety, depression, agitation, libido decreased, nervousness, depersonalisation, nightmare, bruxism (common); suicidal ideation/behaviour, psychotic disorder, thinking abnormal, apathy, hallucination, aggression, euphoric mood, paranoia (uncommon); conversion disorder, paroniria, drug dependence, sleep walking, premature ejaculation (rare).
Nervous system disorders: dizziness, headache, somnolence (very common); tremor, movement disorders (including extrapyramidal symptoms such as hyperkinesia, hypertonia, dystonia, teeth grinding or gait abnormalities), paraesthesia, hypertonia, disturbance in attention, dysgeusia (common); amnesia, hypoaesthesia, muscle contractions involuntary, syncope, hyperkinesia, migraine, convulsion, dizziness postural, coordination abnormal, speech disorder (uncommon); coma, akathisia, dyskinesia, hyperaesthesia, cerebrovascular spasm (including reversible cerebral vasoconstriction syndrome and Call-Fleming syndrome), psychomotor restlessness, sensory disturbance, choreoathetosis, agitation, confusion, diaphoresis, diarrhoea, fever, hypertension, rigidity and tachycardia (rare).
Eye disorders: visual disturbance (common); mydriasis (uncommon); scotoma, glaucoma, diplopia, photophobia, hyphaema, pupils unequal, vision abnormal, lacrimal disorder (rare); maculopathy (not known).
Ear and labyrinth disorders: tinnitus (common); ear pain (uncommon).
Cardiac disorders: palpitations (common); tachycardia, cardiac disorder (uncommon); myocardial infarction, Torsade de Pointes, bradycardia, QTc prolongation (rare).
Vascular disorders: hot flush (common); abnormal bleeding (such as gastrointestinal bleeding), hypertension, flushing, haematuria (uncommon); peripheral ischaemia (rare).
Respiratory, thoracic, and mediastinal disorders: yawning (common); dyspnoea, epistaxis, bronchospasm (uncommon); hyperventilation, interstitial lung disease, laryngospasm, dysphonia, stridor, hypoventilation, hiccups (rare).
Gastrointestinal disorders: nausea, diarrhea, dry mouth (very common); dyspepsia, constipation, abdominal pain, vomiting, flatulence (common); melaena, tooth disorder, oesophagitis, glossitis, haemorrhoids, salivary hypersecretion, dysphagia, eructation, tongue disorder (uncommon); mouth ulceration, pancreatitis, haematochezia, tongue ulceration, stomatitis (rare); colitis microscopic (not known).
Hepatobiliary disorders: hepatic function abnormal, serious liver events (including hepatitis, jaundice and hepatic failure) (rare).
Skin and Subcutaneous Tissue Disorders: hyperhidrosis, rash (common); periorbital oedema, urticaria, alopecia, pruritus, purpura, dermatitis, dry skin, face oedema, cold sweat (uncommon); Stevens-Johnson syndrome and epidermal necrolysis, skin reaction, photosensitivity, angioedema, hair texture abnormal, skin odour abnormal, dermatitis bullous, rash follicular (rare).
Musculoskeletal and connective tissue disorders: back pain, arthralgia, myalgia (common); osteoarthritis, muscle twitching, muscle cramps, muscular weakness (uncommon); rhabdomyolysis, bone disorder (rare); trismus (not known).
Renal and urinary disorders: pollakiuria, micturition disorder, urinary retention, urinary incontinence, polyuria, nocturia (uncommon); urinary hesitation, oliguria (rare).
Reproductive system and breast disorders: ejaculation failure (very common); menstruation irregular, erectile dysfunction (common); sexual dysfunction, menorrhagia, vaginal haemorrhage, female sexual dysfunction (uncommon); galactorrhea, atrophic vulvovaginitis, genital discharge, balanoposthitis, gynaecomastia, priapism (rare); postpartum haemorrhage (not known).
General disorders and administration site conditions: fatigue (very common); malaise, chest pain, asthenia, pyrexia (common); oedema peripheral, chills, gait disturbance, thirst (uncommon); hernia, drug tolerance decreased (rare).
Investigations: weight increased (common); alanine aminotransferase increased, aspartate aminotransferase increased, weight decreased (uncommon); blood cholesterol increased, abnormal clinical laboratory results, semen abnormal, altered platelet function (rare).
Injury and poisoning: injury (common).
Surgical and medical procedures: vasodilation procedure (rare).

DOSAGE AND ADMINISTRATION
Posology
Initial treatment:
Depression and OCD: Sertraline treatment should be started at a dose of 50 mg/day.
Panic Disorder, PTSD, and Social Anxiety Disorder: Therapy should be initiated at a dose of 25 mg/day. After one week, the dose should be increased to 50 mg once daily. This dosage regimen has been shown to reduce the frequency of early treatment emergent side effects characteristic of panic disorder.
Titration
Depression, OCD, Panic Disorder, Social Anxiety Disorder and PTSD: Patients not responding to a 50 mg dose may benefit from dose increases.
Dose changes should be made in steps of 50 mg 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.
Depression: Longer-term treatment may also be appropriate for prevention of recurrence of major depressive episodes (MDE). In most of the cases, the recommended dose in prevention of recurrence of MDE is the same as the one used during current episode. Patients with depression should be treated for a sufficient period of time of at least 6 months to ensure they are free from symptoms.
Panic disorder and OCD: Continued treatment in panic disorder and OCD should be evaluated regularly, as relapse prevention has not been shown for these disorders.
Paediatric patients
Children and adolescents with obsessive compulsive disorder
Age 13-17 years: Initially 50 mg once daily.
Age 6-12 years: Initially 25 mg once daily. The dosage may be increased to 50 mg once daily after one week.
Subsequent doses may be increased in case of less than desired response in 50 mg increments over a period of some weeks, as needed. The maximum dosage is 200 mg daily. However, the generally lower body weights of children compared to those of adults should be taken into consideration when increasing the dose from 50 mg. Dose changes should not occur at intervals of less than one week.
Efficacy is not shown in paediatric major depressive disorder.
No data is available for children under 6 years of age.
Use in elderly: Elderly should be dosed carefully, as elderly may be more at risk for hyponatraemia.
Method of administration
Restraline® should be administered once daily, either in the morning or evening.
Restraline® tablet can be administered with or without food.
Withdrawal symptoms seen on discontinuation of Restraline®
Abrupt discontinuation should be avoided. When stopping treatment with Restraline® the dose should be gradually reduced over a period of at least one to two weeks in order to reduce the risk of withdrawal reactions. 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 physician may continue decreasing the dose, but at a more gradual rate.

OVERDOSAGE
Toxicity: Sertraline has a margin of safety dependent on patient population and/or concomitant medication. Deaths have been reported involving overdoses of sertraline, alone or in combination with other drugs and/or alcohol. Therefore, any overdosage should be medically treated aggressively.
Symptoms: Symptoms of overdose include serotonin-mediated side effects such as somnolence, gastrointestinal disturbances (e.g. nausea and vomiting), tachycardia, tremor, agitation and dizziness. Coma has been reported although less frequently.
QTc prolongation/Torsade de Pointes has been reported following sertraline overdose; therefore, ECG-monitoring is recommended in all ingestions of sertraline overdoses.
Management: There are no specific antidotes to sertraline. It is recommended to establish and maintain an airway and, if necessary, ensure adequate oxygenation and ventilation. Activated charcoal, which may be used with a cathartic, may be as, or more effective than lavage, and should be considered in treating overdose. Induction of emesis is not recommended. Cardiac (e.g. ECG) and vital sign monitoring is also 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.

STORAGE CONDITIONS
Store below 25°C.
Keep in original pack in intact conditions.

Date of revision: October 2023.

Marketing Authorization Holder and Manufacturer:
Benta S.A.L.
Dbayeh-Lebanon

BPI

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