SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

SERLIFE 50

Setraline 50 mg (film coated tablet)

SERLIFE 100

Setraline 100 mg (film coated tablet)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SERLIFE 50

Each tablet contains:

Sertraline hydrochloride equivalent to Sertraline 50 mg

Sugar free

SERLIFE 100

Each film-coated tablet contains:

Sertraline hydrochloride equivalent to Sertraline100 mg

Sugar Free

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablets

SERLIFE 50

White, film-coated, capsule shaped tablets, debossed with `50' on one side and a break line on the other

SERLIFE 100

White, film-coated, capsule shaped tablets, debossed with `100' on one side and a break line on the other

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SERLIFE is indicated for the treatment of

- Major depressive illness such as single episodes and recurrent depression
- Obsessive compulsive disorder (OCD).
- Panic disorders , with or without agoraphobia

SERLIFE is also indicated in the treatment of children aged 13 – 17 with OCD

4.2 Posology and Method of Administration

Adults

Depression: The starting dose is 50 mg daily and the usual antidepressant dose is 50 mg daily. In patients with incomplete response but good toleration at lower doses, dosage adjustments should be made in 50 mg increments over a period of 2 weeks to a maximum of 200 mg daily.

Obsessive Compulsive Disorder: The minimum effective dose is 50 mg daily and doses above 100 mg did not have any additional benefit. 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.

Use in children

The safety and efficacy of **SERLIFE** have not been established in children.

Use in the elderly

No special precautions are required. The usual adult dose is recommended

Panic disorder:

For panic disorder, the minimum recommended effective dose of **SERLIFE** is 50 mg/day. However, therapy for panic disorder should commence at 25 mg/day, increasing to 50 mg/day after one week. This dosage regimen has been demonstrated to reduce the frequency of early treatment emergent side effects characteristic of panic disorder.

Special Populations:

Use in patients with renal or hepatic impairment

SERLIFE should be used with caution in patients with renal and hepatic impairment.(see section 4.3 and 4.4)

Paediatric obsessive-compulsive disorder (OCD):

The administration of **SERLIFE** to paediatric OCD patients (aged 13 – 17) should commence at 50 mg/day. Subsequent doses may be increased in case of lack of response in 50 mg/day increments up to 200 mg 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 SERLIFE, dose changes should not occur at intervals of less than 1 week.

Discontinuation of treatment:

If **SERLIFE** therapy has to be discontinued, **SERLIFE** should be tapered (see section 4.3 and 4.4)

Method of administration

For oral us. **SERLIFE** tablets should be given as a single daily dose with or without food.

4.3 Contraindications

SERLIFE is contra-indicated in patients who have shown hypersensitivity to any of the components of the product.

Concomitant use of **SERLIFE** in patients taking monoamine oxidase inhibitors (MAOIs) including linezolidis contra-indicated (see section 4.4).

Concomitant use in patients taking pimozide is contraindicated (see section 4.5).

Children < 18 years of age with both OCD and a major depressive disorder (see section 4.4).

Use in hepatic or renal insufficiency (see section 4.4).

Pregnancy and lactation as safety has not been established.

4.4 Special warnings and precautions for use

Serotonin Syndrome (SS):

The development of potentially life-threatening syndromes like serotonin syndrome (SS) or Neuroleptic Malignant Syndrome (NMS) has been reported with Selective Serotonin Reuptake Inhibitors (SSRIs), including treatment with Sertraline. The risk of SS or NMS with SSRIs is increased with concomitant use of serotonergic medicines (including triptans and fentanyl and its analogues, tramadol, dextromethorphan, tapentadol, meperidine, methadone and pentazocine), with medicines which impair metabolism of serotonin (including MAOIs), antipsychotics and other dopamine antagonists. SS symptoms 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, diarrhoea). Some signs of SS, including hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes resemble NMS. Patients should be monitored for the emergence of signs and symptoms of SS or NMS syndrome (see section 4.3).

Monoamine oxidase inhibitors:

Cases of serious reactions, sometimes fatal, have been reported in patients receiving medicines containing Sertraline such as **SERLIFE** in combination with a MAOI, including selegiline, moclobemide, linezolid and methylene blue. Some cases presented with features resembling serotonin syndrome. Therefore, **SERLIFE** should not be used in

combination with a MAOI or within 14 days of discontinuing treatment with a MAOI. Similarly, at least 14 days should elapse after discontinuing **SERLIFE** treatment and starting a MAOI (see section 4.3).

Other serotonergic medicines:

Co-administration of medicines containing Sertraline such as **SERLIFE** with other medicines which enhance the effect of serotonergic neurotransmission, such as tryptophan, fenfluramine and fentanyl, or 5-HT antagonists, or the herbal medicine St. John's Wort (*hypericum perforatum*) should be undertaken with caution and avoided whenever possible due to the potential for pharmacodynamic interaction (see section 4.5).

QTc prolongation/Torsade de Pointes (TdP)

Cases of QTc prolongation and Torsade de Pointes (TdP) have been reported during post-marketing use of medicines containing Sertraline such as **SERLIFE**. The majority of reports occurred in patients with other risk factors for QTc prolongation//TdP. Therefore, **SERLIFE** should be used with caution in patients with risk factors for QTc prolongation.

Switching from selective serotonin reuptake inhibitors (SSRIs), antidepressants or anti-obsessional medicines:

There is limited controlled experience regarding the optimal timing of switching from other antidepressants or anti-obsessional medicines to medicines containing Sertraline such as **SERLIFE**. Care and prudent medical judgement should be exercised when switching, particularly from long-acting medicines such as fluoxetine. The duration of a washout period when switching from one SSRI to another has not been established.

Activation of mania/hypomania:

Hypomania or mania may occur in patients treated with medicines containing Sertraline such as **SERLIFE**.

Seizures:

Seizures have been observed in patients using medicines containing Sertaline. These medicines should be avoided in patients with unstable epilepsy and patients with controlled

epilepsy should be carefully monitored. Sertraline containing medicines should be discontinued in any patient who develops seizures.

Suicide/suicidal thoughts or clinical worsening:

All patients treated with medicines containing Sertraline such as **SERLIFE**, in particular those at high risk, should be monitored appropriately and observed closely for clinical worsening and suicidality. Patients, their families, and their caregivers should be encouraged to be alert to the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour especially when initiating therapy or during any change in dose or dosage regimen. The risk of suicide attempt must be considered, especially in depressed patients, and the smallest quantity of medicine, consistent with good patient management, should be provided to reduce the risk of overdose.

Patients with major depressive disorder, both adults and children, may experience worsening of their depression and/or the emergence of suicidal ideation and behaviour, whether or not they are taking antidepressant medicines. This risk may persist until significant remission occurs. A causal role, however, for antidepressant medicine in inducing such behaviour has not been established. Patients being treated with medicines containing Sertraline should, nevertheless, be observed closely for clinical worsening and suicidality, especially at the beginning of a course of therapy or at any time of dose changes, either increases or decreases.

Because of the possibility of co-morbidity between major depressive disorder and other psychiatric and non-psychiatric disorders, the same precautions observed when treating patients with major depressive disorders should be observed when treating patients with other psychiatric and non-psychiatric disorders.

The following symptoms have been reported in patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and non-psychiatric: anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, and mania. Although a causal link between the emergence of suicidal impulses has not been established, consideration should be given

to changing the therapeutic regimen, including possibly discontinuing **SERLIFE**, in patients for whom such symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

If a decision is made to discontinue treatment, **SERLIFE** should be tapered (see section 4.2).

Abnormal bleeding/haemorrhage:

There have been reports of bleeding abnormalities with SSRIs from ecchymoses and purpura to life threatening haemorrhage. Caution is advised in patients taking SSRIs, particularly in concomitant use with medicines 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 (see section 4.5*).*

Hyponatraemia:

Hyponatraemia may occur as a result of treatment with SSRIs such as **SERLIFE**. 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 such as **SERLIFE**. Also, patients taking diuretics or who are otherwise volume-depleted may be at greater risk. Discontinuation of **SERLIFE** should be considered in patients with symptomatic hyponatraemia and appropriate medical intervention should be instituted. Signs and symptoms of hyponatraemia include headache, difficulty concentrating, memory impairment, confusion, weakness and unsteadiness which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest and death.

Bone fractures:

Epidemiological studies show an increased risk of bone fractures in patients receiving serotonin reuptake inhibitors (SRIs) including medicines containing Sertraline such **SERLIFE**. The mechanism leading to this risk is not fully understood.

Use in patients with concomitant illness:

Caution is advisable in using **SERLIFE** in patients with diseases or conditions that could affect metabolism or haemodynamic responses.

SERLIFE has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease.

Use in hepatic insufficiency:

As might be predicted from its primary site of metabolism, liver impairment can affect the elimination of Sertraline containing medicines such as **SERLIFE**. The elimination half-life of Sertraline containing medicines such as **SERLIFE** is prolonged. The use of **SERLIFE** in patients with liver disease must be avoided.

Use in renal insufficiency:

In patients with mild to moderate renal impairment (creatinine clearance 30 – 60 ml/min) or severe renal impairment (creatinine clearance < 30 ml/min), multiple dose pharmacokinetics parameters (AUC or Cmax) are modest. Sertraline containing medicines such as **SERLIFE** should not be used in patients with renal impairment (see section 4.3).

Weak uricosuric effect:

Medicines containing Sertraline such as **SERLIFE** is associated with a mean decrease in serum uric acid of approximately 7 %. The clinical significance of this weak uricosuric effect is unknown.

Diabetes/loss of glycaemic control:

Cases of new onset diabetes mellitus have been reported in patients receiving SSRIs including **SERLIFE**. Loss of glycaemic control including both hyperglycaemia and hypoglycaemia has also been reported in patients with and without pre-existing diabetes. Patients should therefore be monitored for signs and symptoms of glucose fluctuations. Diabetic patients, especially, should have their glycaemic control carefully monitored since their dosage of insulin and/or concomitant oral hypoglycaemic medicine may need to be adjusted.

Laboratory tests:

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

Angle-closure glaucoma:

SSRIs including **SERLIFE** 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 containing medicines such as **SERLIFE** should therefore be used with caution in patients with angle-closure glaucoma or history of glaucoma.

Weight loss:

Significant weight loss may be an undesirable result of treatment with Sertraline containing medicines such as **SERLIFE** for some patients, approximately 0,5 – 1,0 kg weight loss.

Use in children:

The safety and efficacy of Sertraline containing medicicines such as **SERLIFE** have been established in paediatric obsessive-compulsive disorder (OCD) patients aged 13 – 17. Safety and efficacy in the paediatric population other than paediatric patients with OCD have not been established. In clinical trials in major depressive disorder, there were increased reports of hostility and suicide-related adverse events such as suicidal ideation and self-harm (see section 4.3).

Use in geriatrics

No geriatric specific problems have been documented to date with the use of **SERLIFE**.

Withdrawal symptoms:

Abrupt discontinuation of Sertraline containing medicines such as **SERLIFE** may lead to withdrawal symptoms which include dizziness, sweating, nausea, insomnia, tremor, confusion, sensory disturbances, agitation and anxiety.

Effects on ability to drive and use machines:

Sertraline containing medicines such as **SERLIFE** does not cause sedation and does not interfere with psychomotor performance.

Patients should be cautioned when driving a car or operating machinery until they know how **SERLIFE** affects them

4.5 Interaction with other medicines and other forms of Interaction

Monoamine oxidase inhibitors:

The concomitant use of Sertraline containing medicines such as **SERLIFE** with a monoamine oxidase inhibitor (MAOI) is contraindicated. (See sections 4.3 and 4.4).

Pimozide:

Increased pimozide levels have been demonstrated with Sertraline containing medicines such as **SERLIFE** co-administration but were not associated with any changes in ECG. While the mechanism of this interaction is unknown, due to the narrow therapeutic index of pimozide, concomitant administration of **SERLIFE** and pimozide is contraindicated (see section 4.3).

Medicines that prolong the QTc interval:

The risk of QTc prolongation and/or ventricular dysrhythmias (e.g. TdP) is increased with concomitant use of other medicines which prolong the QTc interval (e.g. some antipsychotics and antibiotics) (see section 4.4).

CNS depressants and alcohol:

Co-administration of Sertraline containing medicines such as **SERLIFE** (sertraline 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 **SERLIFE** and alcohol in depressed patients is not recommended.

Lithium:

It is recommended that plasma lithium levels be monitored following initiation of Sertraline therapy such as **SERLIFE**, so that appropriate adjustments to the lithium dose may be

made if necessary. Co-administration with lithium may lead to a higher incidence of 5HT-associated side effects, resulting in an increase in tremor relative to placebo, indicating a possible pharmacodynamic interaction. Therefore, caution is recommended when co-administering **SERLIFE** with medicines such as lithium, which may act via serotonergic mechanisms and patients should be appropriately monitored.

Phenytoin:

Increased phenytoin concentrations may occur when Sertraline containing medicines such as **SERLIFE** and phenytoin are used concomitantly, especially in patients with other medical conditions and/or those receiving multiple concomitant medications. Plasma phenytoin concentrations should be monitored when **SERLIFE** and phenytoin are used concomitantly with appropriate adjustments to the phenytoin dose. In addition, co-administration of phenytoin may cause a reduction of plasma levels of sertraline in **SERLIFE**.

Sumatriptan:

There have been post-marketing reports describing patients with weakness, hyperreflexia incoordination, confusion, anxiety, and agitation following the use of Sertraline containing medicines such as **SERLIFE** and sumatriptan. If concomitant treatment with **SERLIFE** and sumatriptan is clinically warranted, appropriate observation of the patient is advised (see section 4.4 and Other serotonergic medicines below).

Other serotonergic medicines:

Co-administration of Sertraline containing medicines such as **SERLIFE** with other medicines which enhance the effect of serotonergic neurotransmission, such as tryptophan, fenfluramine and fentanyl, 5-HT antagonists, or the herbal medicine St. John's Wort (*hypericum perforatum*) should be undertaken with caution and avoided whenever possible due to the potential for pharmacodynamic interaction (see section 4.4).

Protein-bound medicines:

Sertraline found in **SERLIFE** is highly bound to serum proteins (98 %) in the range of 20 to 500 ng/ml. However, at up to 300 and 200 ng/ml concentrations, respectively, sertraline

and N-desmethylsertraline contained in **SERLIFE** do not alter the plasma protein binding of two other highly protein-bound medicines, viz. warfarin and propranolol. However, in interaction studies with diazepam, tolbutamide and warfarin respectively, Sertraline as found in **SERLIFE** had no significant effects on the protein binding of the substrate (see Warfarin and Other medicine interactions).

Warfarin:

Co-administration of Sertraline containing medicines such as **SERLIFE** 200 mg daily with warfarin resulted in a small but statistically significant increase in prothrombin time. Accordingly, prothrombin time should be carefully monitored when **SERLIFE** therapy is initiated or stopped.

Other medicine interactions:

Co-administration of Sertraline containing medicines such as **SERLIFE** 200 mg daily with diazepam or tolbutamide resulted in small, statistically significant changes in some pharmacokinetic parameters.

Co-administration with cimetidine caused a substantial decrease in **SERLIFE** clearance. The clinical significance of these changes is unknown.

Sertraline containing medicines such as **SERLIFE** has no effect on the beta-adrenergic blocking ability of atenolol. No interaction of Sertraline containing medicines such as **SERLIFE** 200 mg daily was observed with glibenclamide or digoxin.

Electroconvulsive therapy (ECT):

There are no clinical studies establishing the risks or benefits of the combined use of ECT and Sertraline containing medicines such as **SERLIFE**.

Medicines metabolised by cytochrome P450 (CYP) 2D6:

There is variability among antidepressants in the extent of clinically important inhibition of the medicine metabolising isoenzyme CYP 2D6. The clinical significance of this depends on the extent of the inhibition and the therapeutic index of the co-administered medicine. CYP 2D6 substrates with a narrow therapeutic index include tricyclic antidepressants

(TCAs) and class 1C anti-dysrythmics such as propenone and flecainide. In formal interaction studies, chronic dosing with Sertraline containing medicines such as **SERLIFE** 50 mg daily showed minimal elevation of steady state desipramine plasma levels (a marker of CYP 2D6 isoenzyme activity).

Medicines metabolised by other CYP enzymes (CYP 3A3/4, CYP 2C9, CYP 2C19, CYP 1A2):

CYP 3A3/4:

Chronic administration of Sertraline containing medicines such as **SERLIFE** 200 mg daily does not inhibit the CYP 3A3/4 mediated 6-β hydroxylation of endogenous cortisol or the metabolism of carbamazepine. In addition, the chronic administration of Sertraline containing medicines such as **SERLIFE** 50 mg daily does not inhibit the CYP 3A3/4 mediated metabolism of alprazolam. The results of these studies suggest that Sertraline containing medicines such as **SERLIFE** is not a clinically relevant inhibitor of CYP 3A3/4.

CYP 2C9:

The apparent lack of clinically significant effects of the chronic administration of Sertraline containing medicines such as **SERLIFE** 200 mg daily on plasma concentrations of tolbutamide, phenytoin and warfarin suggests that **SERLIFE** is not a clinically relevant inhibitor of CYP 2C9 (see Other medicine interactions, Phenytoin and Warfarin).

CYP 2C19:

The apparent lack of clinically significant effects of the chronic administration of Sertraline containing medicines such as **SERLIFE** 200 mg daily on plasma concentrations of diazepam suggests that **SERLIFE** is not a clinically relevant inhibitor of CYP 2C19 (see Other medicine interactions).

CYP 1A2:

In vitro studies indicate that Sertraline containing medicines such as **SERLIFE** has little or no potential to inhibit CYP 1A2.

4.6 Fertility, pregnancy and lactation

Pregnancy: Adequate and well-controlled studies in pregnant women have not been performed. Animal reproduction studies have not shown any evidence of teratogenicity or embryotoxicity with sertraline. However, since animal reproduction studies are not always predictive of human response, **SERLIFE** should be used during pregnancy only if the potential benefits outweigh the risks. Women of childbearing potential who are on **SERLIFE** should employ an adequate method of contraception.

Lactation: Limited data concerning sertraline levels in breast milk are available, hence use of **SERLIFE** in breast feeding mothers is not recommended

4.7 Effects on ability to drive and use machines

Since antidepressant or anti-obsessional medicines may impair the abilities required to perform potentially hazardous tasks such as driving a car or operating machinery, the patient should be cautioned accordingly

4.8 Undesirable effects

MedDRA System Organ Class	Frequent	Less Frequent	Frequency Unknown
Infections and infestations	- Pharyngitis	- Upper respiratory tract infection - Rhinitis - Diverticulitis - Gastroenteritis - Otitis media	
Neoplasms benign, malignant (including cysts and polyps)		- Neoplasm	
Blood and lymphatic system disorders		- Lymphadenopathy - Leucopenia - Thrombocytopenia	
Immune system disorders		- Hypersensitivity - Allergic reaction - Allergy - Anaphylactoid reaction	
Endocrine disorders		- Hypothyroidism - Hyperprolactinemia	

		- Inappropriate antidiuretic hormone secretion	
Metabolism and nutrition disorders	- Anorexia - Decreased appetite - Increased appetite*	- Hyponatremia - Diabetes mellitus - Hypercholesterolaemia - Hypoglycaemia	- Hyperglycaemia
Psychiatric disorders	- Insomnia - Depression* - Depersonalisation - Nightmare - Agitation - Anxiety - Nervousness - Decreased libido* - Bruxism - Suicidal Ideation/Behaviour - Suicide Attempts	- Depressive symptoms - Euphoric mood* - Hallucination* - Aggression* - apathy - Abnormal thinking - Paroniria - Psychosis - Conversion disorder - Medicine dependence - Psychotic disorder* - Paranoia - Sleep walking - Premature ejaculation	
Nervous system disorders	- Dizziness - Somnolence - Insomnia - Headache* - Hypoaesthesia* - Movement disorders including extrapyramidal	- Convulsion* - Involuntary muscle contractions* - Abnormal coordination - Hyperkinesia - Amnesia - Speech disorder - Postural dizziness	- Akathisia and psychomotor restlessness (see section 4.4) - cerebrovascular spasm (including

	symptoms such as hyperkinesia, hypertonia, dystonia, teeth grinding or gait abnormalities), paraesthesia*, tremor, hypertonia, dysgeusia, disturbance in attention	- Migraine* - Syncope - Coma* - Choreoathetosis - Dyskinesia - Hyperaesthesia - Sensory disturbance - Signs and symptoms associated with Serotonin Syndrome or Neuroleptic Malignant Syndrome	reversible cerebral vasoconstriction syndrome and Call-Fleming syndrome)
Eye disorders	- Vision Abnormal - Visual disturbance	- Mydriasis* - Glaucoma - Lacrimal disorder - Scotoma - Diplopia - Photophobia - Hyphaema	-Unequal pupils
Ear and labyrinth disorders	- Tinnitus*	- Ear pain	
Cardiac disorders	- Palpitations*	- Tachycardia - Myocardial infarction - Bradycardia - Cardiac disorder	- QTc prolongation - Torsade de Pointes
Vascular disorders	- Hot flush*	- Hypertension* - Flushing - Peripheral ischaemia - Haematuria	

		- Abnormal bleeding (such as gastrointestinal bleeding)	
Respiratory, thoracic and mediastinal disorders	- Yawning* - Rhinitis - Pharyngitis	- Bronchospasm* - Dyspnoea - Epistaxis - Laryngospasm - Hyperventilation - Hypoventilation - Stridor - Dysphonia, - Hiccups	- Interstitial lung disease
Gastrointestinal disorders	- Diarrhoea/loose stools - -Dry mouth - Nausea - Abdominal pain* - Constipation* - Dyspepsia - Vomiting* - Flatulence	- Oesophagitis - Dysphagia - Haemorrhoids - Salivary - Hypersecretion - Tongue disorder - Eructation - Melaena - Haematochezia - Stomatitis - Tongue ulceration - Tooth disorder - Glossitis - Mouth ulceration - Pancreatitis	-

Hepatobiliary disorders		- Abnormal hepatic function - Serious liver events (including hepatitis, jaundice, and hepatic failure)	
Skin and subcutaneous tissue disorders	- Hyperhidrosis - Rash*	- Alopecia* - Periorbital oedema* - Pruritus - Purpura* - Face oedema - Cold sweat - Dry skin - Urticaria* - Angioedema - Photosensitivity skin reaction - Severe cutaneous adverse reactions (SCAR) e.g. Stevens-Johnson syndrome and epidermal necrolysis, dermatitis, bullous dermatitis, follicular rash, abnormal hair texture, abnormal skin odour	

Musculoskeletal and connective tissue disorders	- Arthralgia - Myalgia	- Muscle cramps - Osteoarthritis - Muscular weakness - Back pain - Muscle twitching - Bone disorder	
Renal and urinary disorders		- Urinary incontinence* - Nocturia - Urinary retention* - Polyuria - Pollakiuria - Micturition disorder - Oliguria - Urinary hesitation	
Reproductive system and breast disorders	- Ejaculation failure - Erectile dysfunction - IrregularMenstruation	- Vaginal haemorrhage - Sexual dysfunction - Female sexual dysfunction - Menorrhagia - Atrophic vulvovaginitis - Balanoposthitis - Genital discharge - Galactorrhoea* - Gynaecomastia - Priapism*	
General disorders and administration site conditions	- Fatigue* - Asthenia* - Chest pain* - Malaise*	- Peripheral oedema - Chills - Pyrexia* - Thirst	

		- Hernia - Decreased medicine tolerance - Gait disturbance	
Investigations		- Increased alanine aminostransferase (ALT)* - increased aspartate aminotransferase (AST)* - decreased weight* - increased weight* - Abnormal semen - Abnormal clinical laboratory results - Altered platelet function - Increased blood cholesterol	
Injury, poisoning and procedural complications		- Injury	
Surgical and medical procedures		- Vasodilation procedure	
Other		- Symptoms Following the discontinuation of sertraline	

		containing medicines such as **SERLIFE** have been reported and included agitation, anxiety, dizziness, headache, nausea, paraesthesia	

*These adverse reactions also occurred in post-marketing experience (frequency not known)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Sertraline containing medicines such as **SERLIFE** has a wide margin of safety. No serious sequelae have been reported following sertraline overdose as high as 6 g. Symptoms of

overdose include serotonin-mediated side effects such as electrocardiogram QT prolonged, Torsade de Pointes, somnolence, gastrointestinal disturbances (such as nausea and vomiting), tachycardia, tremor, agitation and dizziness. Less frequently reported was coma Although there have been no reports of death due to sertraline-only overdose, fatalities have occurred in combination with other medicines and/or alcohol. No specific therapy is recommended and there is no specific antidote to **SERLIFE**. Treatment is essentially symptomatic and supportive, possibly including:

-Establishing and monitoring airway.

-Ensuring adequate oxygenation and ventilation.

-Monitoring cardiac function and vital signs.

Administering activated charcoal, which may be used with sorbitol, may be as or more effective than emesis or gastric lavage.

Dialysis, forced diuresis, haemoperfusion and exchange transfusions are unlikely to be of benefit due to **SERLIFE** large volume of distribution and high degree of protein binding.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Sertraline, a naphthaleneamine derivative, is a selective serotonin reuptake inhibitor (SSRI). Sertraline has only weak effects on neuronal reuptake of norepinephrine and dopamine. Chronic administration of sertraline in animals has resulted in downregulation of post-synaptic β-adrenergic receptors. Sertraline's inhibition of serotonin reuptake enhances serotonergic transmission, which results in subsequent inhibition of adrenergic activity in the locus ceruleus. Sertraline has no specific affinity for adrenergic (α_1, α_2, or β) receptors, muscarinic cholinergic receptors, γ-aminobutyric acid receptors, dopaminergic receptors, histaminergic receptors, serotonergic ($5HT_{1A}$, $5HT_{1B}$, $5HT_2$) or benzodiazepine receptors. Sertraline does not inhibit monoamine oxidase

The chronic administration of sertraline in animals was associated with down regulation of brain norepinephrine (noradrenaline) receptors.

5.2 Pharmacokinetic properties

After oral administration, sertraline is slowly absorbed. It undergoes rapid first pass metabolism. The C_{max} and the AUC are proportional to the dose over the range of 50-200 mg of sertraline, demonstrating linear pharmacokinetics. Sertraline undergoes extensive first pass metabolism in the liver. After once-daily dosing of sertraline, steady state plasma concentrations are reached in about 7 days in adult subjects and after 2-3 weeks in older patients. The primary initial pathway of sertraline metabolism is N-demethylation to form N-desmethylsertraline, which is substantially less active than the parent compound, exhibiting only about $1/8^{th}$ of its activity. Both sertraline and desmethylsertraline undergo oxidative deamination and subsequent reduction, hydroxylation, and glucuronide conjugation. The elimination half-lives of sertraline and desmethylsertraline are 24-26 and 62-104 hours respectively. Both sertraline and its metabolite, desmethylsertraline are extensively distributed into the tissues, the volume of distribution for the parent compound being about 76 l/kg. The plasma protein binding is greater than 98%. About 40-45% of an administered radioactive dose was recovered in the urine within 9 days with less than 0,2% recovered unchanged; faecal recovery is 40-45%, including 12-14% unchanged sertraline. The clearance of sertraline is about 38 $\pm$ 14 ml/min/kg in healthy, young subjects which is decreased by about 40% in older individuals. Clearance of desmethylsertraline is also decreased in older men but not in older women.

The pharmacokinetics of sertraline have not been studied in

Patients with significant renal impairment.

Since sertraline is extensively metabolised in the liver, its

Metabolism may be altered in hepatic function impairment.

Therefore caution is advised when sertraline administered to such patients; a lower dose or less frequent dosing should be considered.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydrogen phosphate, hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose (PH 101), microcrystalline cellulose (PH 102), purified water, sodium starch glycollate.

Film-coating

Opadry-OY-S-58910(White):

Hypromellose

Titanium Dioxide(Cl No.77891

Macrogol 400

Talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store at or below 25 ^{0}C.

Protect from moisture.

Do not remove the blisters from the carton until required for use.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

Serlife 50 Tablets: Tablets are packed in blister strips.

Carton containing 30 or 100 tablets.

Serlife 100 Tablets: Tablets are packed in blister strips

Carton containing 30 or 100 tablets.

The blister material is a white, opaque PVC film with a backing of aluminium foil.

6.6 Special precautions for disposal

Return all unused or expired medicines to your pharmacist for safe disposal. Do not dispose of unused medicines in drains or sewage systems (e.g. toilets)

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy (SA) (Pty) Ltd

Ground Floor, Tugela House

Riverside Office Park

1303 Heuwel Avenue

Centurion, Pretoria

Gauteng

South Africa

8. REGISTRATION NUMBER(S)

SERLIFE 50: Will be allocated by SAHPRA upon registration

SERLIFE 100: Will be allocated by SAHPRA upon registration

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Will be allocated by SAHPRA upon registration

10. DATE OF REVISON OF THE TEXT

References
• Prescribing Information of Zoloft® (sertralined) 50mg, PFIZER LABORATORIES (Pty) Limited, Sandton, June 2017.