PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Lustral® Tablets 50 mg
Lustral® Tablets 100 mg
Film-coated tablets

Each tablet contains:

Sertraline (as hydrochloride) 50 mg or 100 mg

For a list of inactive ingredients and allergens in this preparation, see section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

This medicine is not intended for use in children and adolescents under 18 years of age.

What should I know about the medicine?

Antidepressants and anti-anxiety medicines increase the risk of suicidal behavior and thoughts in children, adolescents and young adults up to the age of 25.

When starting treatment with the medicine, patients of all ages and their relatives should monitor behavioral changes such as: worsening of depression, suicidal thoughts, aggression and the like.

If changes such as these occur, refer to the doctor immediately (see section 2).

1. WHAT IS THE MEDICINE INTENDED FOR?

A medicine intended for the treatment of symptoms of depression in patients with or without a history of mania. After achieving a satisfactory response, continued treatment with the medicine is effective in preventing relapse of the initial depressive episode or recurrence of further depressive episodes.

Therapeutic group:
This medicine belongs to the SSRI group, selective serotonin reuptake inhibitors.

2. BEFORE USING THE MEDICINE

Do not use this medicine if:

- × You are sensitive (allergic) to the active ingredient or any of the additional ingredients contained in the medicine (listed in section 6).
- × You are taking, or have taken, monoamine oxidase inhibitors (MAOI) (such as: selegiline, moclobemide) or MAOI-like drugs (such as: linezolid). Wait at least one week after completing treatment with sertraline and starting treatment with MAOIs. Similarly, wait at least two weeks after completing treatment with MAOIs and beginning treatment with sertraline.

×	You are concomitantly taking a medicine called pimozide (a medicine intended for mental disorders such as psychosis).

Special warnings regarding use of the medicine

Before treatment with Lustral®, tell the doctor if:

- You are suffering, or have suffered in the past, from epilepsy or have a history of seizures. Tell the doctor immediately if a seizure occurs.
- You have suffered in the past from manic depressive disorder (bipolar disorder) or schizophrenia. Tell the doctor immediately if you have a manic episode.
- You have or have had thoughts of harming yourself or suicidal thoughts (see below in this section **"Suicidal thoughts and worsening of your depression or anxiety disorder"**).
- You have Serotonin Syndrome. In rare cases this syndrome may occur when you are taking certain medicines at the same time as this preparation (for symptoms, see section 4 "Side effects"). Your doctor will have told you if you have suffered from this syndrome in the past.
- You have low blood sodium levels, since treatment with Lustral® may cause this. Tell the doctor if you are taking certain medicines to treat hypertension, as these medicines can also alter the sodium level in your blood. Be particularly careful in elderly people; they are at higher risk.
- You have liver disease. In this case, the doctor may decide to lower the dosage of the medicine administered.
- You have diabetes. Taking this preparation may affect your blood glucose levels and there may therefore be a need to adjust the dosage of your anti-diabetes medicines.
- You have a history of bleeding disorders (tendency to develop bruises), or if you are pregnant (see "Pregnancy, breastfeeding and fertility" section) or have been taking medicines which thin the blood (such as: acetylsalicylic acid (aspirin), or warfarin) or may increase the risk of bleeding.
- You are having electroconvulsive therapy (ECT).
- You have eye problems, such as certain kinds of glaucoma (increased intraocular pressure).
- You have an abnormality of your heart tracing after an electrocardiogram (ECG) known as prolonged QT interval.
- If you have heart disease, low potassium levels or low magnesium levels, family history of QT interval prolongation, slow heart rate and concomitant use of medications which prolong QT interval.

Akathisia/Restlessness:
Use of the medicine has been linked to a distressing restlessness and need to move, often with inability to sit or stand still (akathisia). This effect is most likely to occur during the first weeks of treatment. Increasing the dosage may be harmful so if you develop such effects, you should talk to your doctor.

Withdrawal reactions:
Side effects relating to stopping treatment (withdrawal reactions) are common, particularly if the treatment is stopped suddenly (see sections 3 and 4). The risk of withdrawal symptoms depends on the length of treatment, dosage, and the rate at which the dosage of the medicine is reduced. Generally, the severity of these symptoms is mild to moderate. However, these symptoms can be serious in some patients. These symptoms mostly occur within the first few days after stopping treatment. In general, such symptoms wear off on their own and gradually disappear within 2 weeks. In some patients they may last longer (2-3 months or even more). When stopping treatment with this medicine, it is recommended to reduce the dosage gradually over a period of several weeks or months, and you should always discuss the best way of stopping treatment with the doctor.

Suicidal thoughts and worsening of your depression or anxiety disorder:

If you are depressed and/or have anxiety disorders, you can sometimes have thoughts of harming yourself or suicidal thoughts. These effects may occur more when first starting antidepressants, since it takes time until they begin to have an effect, usually about two weeks but sometimes even longer.

You may be more likely to think like this:

- **If you have previously had suicidal thoughts or thoughts about harming yourself.**
- **If you are a young adult.** Data from clinical trials have shown an increased risk of suicidal behavior in adults aged less than 25 years with psychiatric conditions who were treated with an antidepressant.

If you have thoughts of harming yourself or suicidal thoughts at any time, contact your doctor or go to a hospital straight away.

You may find it helpful to tell a relative or close friend that you are depressed or have an anxiety disorder and ask them to read this leaflet. You might ask them to tell you if they think your depression or anxiety disorder is getting worse, or if they are worried about changes in your behavior.

Sexual problems
Medicines like Lustral® (also called SSRIs) may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms have continued after stopping treatment.

Children and adolescents
Lustral® is not intended for children and adolescents under the age of 18 years.

Drug Interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines or dietary supplements, tell the doctor or pharmacist.

Some medicines may affect the way Lustral® works, or Lustral® itself can reduce the effectiveness of other medicines taken at the same time.

Do not use Lustral® if you are being treated with the following medicines:

Medicines called monoamine oxidase inhibitors (MAOIs), such as: moclobemide (to treat depression) and selegiline (to treat Parkinson's disease), linezolid (antibiotic), methylene blue (to treat high levels of methemoglobin in the blood), medicines to treat mental disorders such as psychosis (pimozide). Taking Lustral® together with these medicines may cause serious side effects.

Tell your doctor if you are taking the following medicines:

- Medicines containing amphetamines (used to treat attention deficit hyperactivity disorder (ADHD), narcolepsy and obesity).
- Preparations containing the *Hypericum* herb (St. John's Wort) – the effect of the *Hypericum* herb may last for 1-2 weeks.
- Products containing the amino acid tryptophan.
- Medicines to treat severe pain (such as: tramadol).
- Medicines used in anesthesia or to treat chronic pain (such as: fentanyl, mivacurium and succinylcholine).
- Preparations to treat migraines (such as: sumatriptan).
- Blood thinning medicines (warfarin).
- Medicines to treat pain/arthritis (nonsteroidal anti-inflammatory drugs [NSAID's], such as: ibuprofen, acetylsalicylic acid [aspirin]).
- Sedatives (diazepam).
- Diuretics.
- Medicines to treat epilepsy (phenytoin, phenobarbital, carbamazepine).

- Medicines to treat diabetes (tolbutamide).
- Medicines to treat excessive acidity, peptic ulcer or heartburn (cimetidine, omeprazole, lansoprazole, pantoprazole, rabeprazole).
- Medicines to treat mania and depression (lithium).
- Other medicines to treat depression (such as: amitriptyline, nortriptyline, nefazodone, fluoxetine, fluvoxamine).
- Medicines to treat schizophrenia and other mental disorders (such as: perphenazine, levomepromazine or olanzapine).
- Medicines used to treat hypertension, chest pain or to regulate the rate and rhythm of the heart (such as: verapamil, diltiazem, flecainide, propafenone).
- Medicines used to treat bacterial infections (such as: rifampicin, clarithromycin, telithromycin, erythromycin).
- Medicines used to treat fungal infections (such as: ketoconazole, itraconazole, posaconazole, voriconazole, fluconazole).
- Medicines to treat HIV/AIDS and hepatitis C (protease inhibitors such as: ritonavir, telaprevir).
- Medicines used to prevent nausea and vomiting after an operation or chemotherapy (aprepitant).
- Medicines known to increase the risk of changes in the electrical activity of the heart (such as: antipsychotics and certain antibiotics).

Use of the medicine and food
The medicine can be taken with or without food. Swallow the tablet with a little water.
Do not drink grapefruit juice during the treatment with the medicine, as it may cause an increase in the level of the medicine in the blood.

Use of the medicine and alcohol consumption
Avoid consumption of alcohol during the treatment with the medicine.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning a pregnancy, consult with your doctor before using this medicine.
The safety of Lustral® has not been fully established in pregnant women. Lustral® will only be given during pregnancy if your doctor considers that the benefit is greater than any possible risk to the fetus.

If you take Lustral® near the end of your pregnancy there may be an increased risk of heavy vaginal bleeding shortly after birth, especially if you have a history of bleeding disorders.
Inform your doctor or midwife that you are taking Lustral® during pregnancy so that they can advise you. Taking it during pregnancy, particularly in the last 3 months of pregnancy, may increase the risk of a serious condition in newborns, called persistent pulmonary hypertension of the newborn (PPHN). This condition makes the baby breathe faster and appear bluish. These symptoms usually begin during the first 24 hours after the baby is born. If this happens to your baby, refer to your doctor immediately.
Other symptoms the newborn baby may have, usually appear during the first 24 hours after birth. The symptoms include: trouble breathing, blue discoloration of the skin, skin that is too cold or too hot, blue lips, vomiting or feeding problems, excessive tiredness, sleeping difficulties, continuous crying, stiff or floppy muscles, tremors, jitters or fits, increased reflex reactions, irritability, decrease in blood sugar level.
If you notice that your baby has any of these symptoms after the birth, or you are concerned about your baby's condition, contact the doctor.
Evidence shows that Lustral® is secreted into breast milk. Do not use Lustral® if you are breastfeeding, unless the doctor considers that the benefit from the medicine exceeds any possible risk to your baby.
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Studies performed in animals have demonstrated that some medicines such as Lustral® may reduce the quality of sperm. Theoretically, this may affect fertility, but no impact on human fertility has been observed as yet.

Driving and using machines
Use of this medicine may impair your ability to drive or operate machinery. Therefore, do not drive a vehicle or operate dangerous machinery until you know how the medicine affects your ability to perform these activities.

Important information about some of this medicine's ingredients
Lustral® contains sodium.
Lustral® contains less than 1 millimole (23 mg) sodium per 50 mg and 100 mg film-coated tablet, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use this medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

The standard dosage is usually: 50 mg once a day, in the morning or the evening. The daily dosage may be increased in increments of 50 mg and at time intervals of at least one week over a period of weeks. The maximum recommended dosage is 200 mg once a day.

Your doctor will instruct you how long to take this medicine. This depends on the nature of your illness and how well you respond to treatment.

An improvement in your symptoms may only occur after several weeks. Usually, treatment of depression should continue for 6 months after improvement.

If you have liver or kidney problems, inform your doctor, and follow his treatment instructions.

Do not exceed the recommended dose!

The medicine can be taken with or without food.

Lustral® 50 mg tablets: The tablet can be halved. There is no information regarding crushing/chewing.

Lustral® 100 mg tablets: There is no information regarding crushing/halving/chewing.

If you accidentally took a higher dosage
If you took an overdose, or if a child has accidentally swallowed some medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you. Signs of overdose can include: drowsiness, nausea and vomiting, rapid heart rate, agitation, shaking, dizziness and in rare cases loss of consciousness.

If you forgot to take the medicine
If you forgot to take this medicine at the required time, skip the forgotten dose and take the next dose at the scheduled time. Never take a double dose to compensate for the forgotten dose!
Adhere to the treatment as recommended by the doctor.

If you stop taking the medicine
Even if there is an improvement in your health condition, do not stop treatment with the medicine without consulting the doctor. The doctor will instruct you how to stop the treatment gradually over several weeks, before you finally stop taking the medicine. Abrupt discontinuation of the medicine may be accompanied by effects such as: dizziness, numbness, sleeping disturbances, anxiety or agitation, headaches, nausea and vomiting, shaking. If you experience any of these side effects or other side effects upon discontinuation of the treatment, please inform the doctor.

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Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of this medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Lustral® may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Nausea is the most common side effect. Side effects are dose-dependent and usually disappear or lessen with continued treatment.

Tell the doctor immediately:

If you experience any of the following symptoms after taking this medicine, these symptoms can be serious.

- If you develop a severe skin rash that causes blistering (erythema multiforme) (this can also affect the mouth and tongue). These may be signs of Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis. Your doctor will stop your treatment in these cases.
- Allergic reaction or allergy, which may include symptoms such as: an itchy skin rash, breathing difficulties, wheezing, swollen eyelids, face or lips.
- If you experience agitation, confusion, diarrhea, high temperature, high blood pressure, excessive sweating and rapid heartbeat. These are symptoms of Serotonin Syndrome. In rare cases this syndrome may occur when you are taking certain medicines at the same time as this medicine. In this case, your doctor may stop your treatment.
- If your skin and eyes turn yellow, which may be indicative of liver damage.
- If you experience depressive symptoms with thought of harming yourself or suicidal thoughts.
- If you start to get feeling of restless and are not able to sit or stand still after you started to take this medicine. You should tell the doctor if you start to feel restless.
- If you have a fit (seizure).
- If you had a manic episode (see section 2 “Special warnings regarding use of the medicine”).

The following side effects were seen in clinical trials in adults and during use of the medicine after marketing:

Very common side effects (may appear in more than 1 in 10 people):

Insomnia, dizziness, sleepiness, headache, diarrhea, nausea, dry mouth, ejaculation failure, fatigue.

Common side effects (may appear in up to 1 in 10 people):

- common cold, sore throat, runny nose
- decreased appetite, increased appetite
- anxiety, depression, agitation, decreased sexual interest, nervousness, feeling strange, nightmare, teeth grinding
- shaking, muscular movement problems (such as moving a lot, tense muscles, difficulty walking, muscle stiffness, spasms and involuntary movements of muscles)*, numbness and tingling, muscle tension, lack of attention, abnormal taste
- visual disturbances
- ringing in ears
- palpitations
- hot flushes

- yawning
- upset stomach, constipation, abdominal pain, vomiting, gas
- increased sweating, rash
- back pain, joint pain, muscle pain
- menstrual irregularities, erectile dysfunction
- malaise, chest pain, weakness, fever
- weight increased
- injury

Uncommon side effects (may appear in up to 1 in 100 people):

- gastroenteritis, ear infection
- tumor
- hypersensitivity, seasonal allergy
- low thyroid hormone levels
- suicidal thoughts, suicidal behavior*, psychotic disorder, thinking abnormal, apathy, hallucination, aggression, euphoric mood, paranoia
- amnesia, decreased feeling, involuntary muscle contractions, passing out, moving a lot, migraine, convulsion, dizziness while standing up, abnormal coordination, speech disorder
- dilated pupils
- ear pain
- fast heartbeat, heart problem
- bleeding (such as: stomach bleeding)*, high blood pressure, flushing, blood in urine
- shortness of breath, nose bleed, breathing difficulty, wheezing
- tarry stools, teeth disorder, inflammation of the esophagus, tongue problems, hemorrhoids, increased saliva, difficulty swallowing, burping, tongue disorder
- eye swelling, hives, hair loss, itching, purple spots on skin, skin problem with blisters, dry skin, face swelling, cold sweat
- osteoarthritis, muscle twitching, muscle cramps*, muscular weakness
- increase in frequency of urination, difficulty urinating, unable to urinate, urinary incontinence, increase in urination, nighttime urination
- sexual dysfunction in men and women, excessive vaginal bleeding, vaginal hemorrhage
- swelling of legs, chills, difficulty walking, thirst
- increase in liver enzyme levels, decreased weight
- **Cases of suicidal thoughts and behavior have been reported during the treatment with Lustral® or just after discontinuation of the treatment with Lustral® (see section 2).**

Rare side effects (may appear in up to 1 in 1,000 people):

- diverticulitis, swollen lymph glands, decrease in number of platelets*, decrease in number of white blood cells*
- severe allergic reaction
- endocrine problems*
- high cholesterol, problems controlling blood sugar levels (diabetes), low blood sugar level, increase in blood sugar levels*, low blood sodium level*
- physical symptoms due to stress or emotions, terrifying abnormal dreams*, drug dependence, sleep walking, premature ejaculation

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- coma, abnormal movements, difficulty moving, increased sensation, sudden severe headache (may be a sign of a serious condition involving reversible constriction of cerebral blood vessels)*, sensory disturbance
- spots in front of eyes, glaucoma, double vision, light hurts eye, blood in the eye, unequal sized pupils*, abnormal vision*, tear problem
- heart attack, light-headedness, fainting, or chest discomfort which could be signs of changes in the electrical activity (seen on electrocardiogram) or abnormal rhythm of the heart*, slow heartbeat
- poor circulation in limbs
- breathing fast, progressive scarring of lung tissue (interstitial lung disease)*, closing up of throat, difficulty talking, slow breathing, hiccups
- mouth ulcers, pancreatitis*, blood in stool, tongue ulcers, sore mouth
- problems with liver function, serious liver function impairment*, yellowing of the skin and eyes (jaundice)*
- skin reaction to sun*, skin edema*, abnormal hair texture, skin odor abnormal, hair follicle rash, breakdown of muscle tissue*, bone disorder
- urinary hesitation, decreased urination
- breast discharge, vaginal dryness, genital discharge, red painful penis and foreskin, breast enlargement*, prolonged erection
- hernia, decreased drug tolerance
- increase in blood cholesterol levels, abnormal laboratory tests*, abnormal semen, problems with clotting*
- relaxation of blood vessels

Side effects of unknown frequency (effects whose frequency has not been determined):

- lockjaw*
- bedwetting*
- partial loss of vision
- inflammation of the colon (causing diarrhea*)
- heavy vaginal bleeding shortly after birth (postpartum hemorrhage), see "Pregnancy, breastfeeding and fertility" in section 2 for more information*

Side effects reported during use of the medicine, after marketing began, are marked by an *.

Symptoms that may occur in the case of discontinuation of treatment

If you suddenly stop taking the medicine, you may experience side effects such as: dizziness, numbness, sleep disturbances, agitation or anxiety, headaches, nausea, vomiting and shaking (see section 3).

An increased risk of bone fractures has been observed in patients taking this type of medicines.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

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- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use this medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions

- Store the medicine below 25°C.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Microcrystalline cellulose, calcium hydrogen phosphate dihydrate, sodium starch glycollate, hydroxypropyl cellulose, magnesium stearate, purified water, white opadry, clear opadry.

What the medicine looks like and the contents of the package:

Lustral® tablets 50 mg: a white, film-coated, capsule-shaped tablet with a score line, with 'ZLT50' marked on one side and 'PFIZER' marked on the other side.

Lustral® tablets 100 mg: a white, film-coated, capsule-shaped tablet with 'ZLT100' marked on one side and 'PFIZER' marked on the other side.

The tablets are packaged in blisters of 20 or 28 tablets per pack. Not all package sizes may be marketed.

Registration holder's name and address: Pfizer P.F.E Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach, 46725.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Lustral® tablets 50 mg: 120.51.27480

Lustral® tablets 100 mg: 120.52.27481

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