PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

Venla 37.5; 75
Tablets

Composition:
Venla 37.5: Each tablet contains: Venlafaxine 37.5 mg as the hydrochloride salt
Venla 75: Each tablet contains: Venlafaxine 75 mg as the hydrochloride salt
Inactive and allergenic ingredients in the medicine: see section 6 "Further information" and "Important information regarding some of the ingredients of the medicine" in section 2.
Read the 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 for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

Antidepressants and antianxiety medicines increase the risk for suicidal behavior and thoughts in children, adolescents and young adults up to the age of 25.
When starting treatment, patients of all ages and their relatives must monitor for behavioral changes, such as: worsened depression, suicidal thoughts, aggressiveness, and the like. If these changes apply to you, refer to a doctor immediately (see section 2 "Before using the medicine").

1. WHAT IS THE MEDICINE INTENDED FOR?
Venla is an antidepressant that belongs to the SNRIs (Serotonin Noradrenaline Reuptake Inhibitors) antidepressant group.
This group of medicines is used to treat depression. The mechanism of action of antidepressants is not fully understood; the medicines can impact the rise in serotonin and noradrenaline levels in the brain.
Venla is intended to treat adults suffering from depression. It is very important that depression be treated. Without treatment, your condition may not pass and may even worsen, such that it will be difficult to treat in the future. The medicine **Venla** is not intended for the treatment of children and adolescents below the age of 18.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- you are sensitive (allergic) to the active ingredient (venlafaxine) or to any of the additional ingredients contained in the medicine (see section 6: "Further information").
- You are taking, or have taken in the past 14 days, nonreversible monoamine oxidase inhibitors (MAOIs) used to treat depression and Parkinson's disease. Taking nonreversible MAOIs with **Venla** may cause serious and life-threatening side effects. In addition, wait at least 7 days after discontinuing of treatment with **Venla** before starting treatment with MAOIs. See "Drug interactions" section and information in this section about "Serotonin syndrome".

Special warnings regarding use of the medicine
Before treatment with Venla, tell the doctor if:
- you are taking other medicines that increase the risk of serotonin syndrome when taken together with **Venla** (see section 2, subsection "Drug interactions").
- you are suffering from eye diseases, such as certain types of glaucoma (increased ocular pressure).
- you are suffering, or have suffered in the past, from hypertension.
- you are suffering, or have suffered in the past, from heart diseases.
- you have been told that you are suffering from irregular heart rate.
- you have suffered in the past from seizures (convulsions).
- you have suffered from low blood sodium levels (hyponatremia).
- you have a tendency to develop bruises (hematomas under the skin) or to bleed easily (history of bleeding problems), or if you are taking medicines that may increase the risk of bleeding, such as warfarin (to prevent blood clots).
- you or a close relative has suffered in the past from mania or bipolar disorder (overexcitedness or euphoria).
- you have a history of aggressive behavior.
- **Venla** may cause restlessness or inability to sit or stand still during the first few weeks of treatment. Tell the doctor if you are suffering from this condition.
- Suicidal thoughts and worsening of your depression or anxiety disturbance:
  If you are depressed and/or suffer from an anxiety disorder, you may have thoughts of harming or killing yourself.
  These thoughts may worsen when starting to use antidepressants, as it takes time for these medicines to begin to work, usually approximately two weeks and sometimes even longer.
  There may be a higher likelihood of having these thoughts if:
  - you have had thoughts of killing or hurting yourself in the past.
  - you are a young adult. Information from clinical trials has shown that there is an increased risk of suicidal behavior among young adults (under 25 years of age) with psychiatric conditions who were treated with antidepressants.

  If you have thoughts of hurting or killing yourself at any time, contact your doctor or proceed immediately to a hospital emergency room.
  It may be helpful to tell a relative or friend if you are suffering from depression or an anxiety disorder and to ask them to read this leaflet. Ask them if they think your depression or anxiety has worsened or if they are concerned about changes in your behavior.
- Dry mouth: Dry mouth has been reported in 10% of patients treated with venlafaxine. This condition may increase the risk of caries, and therefore, dental hygiene should be strictly maintained.
- Diabetes: The blood glucose level may change due to treatment with **Venla**; therefore, if you have diabetes, consult with the doctor about adjusting the dosage of the diabetes medicines.
- Sexual dysfunction: Medicines such as **Venla** (called serotonin and noradrenaline reuptake inhibitors [SNRIs]) can cause symptoms of sexual dysfunction (see section 4 "Side effects"). In some cases, these symptoms persisted after stopping treatment.

Children and adolescents
The medicine is not recommended for use in children and adolescents under 18 years of age.
In addition, you must know that patients under 18 years of age are at higher risk of side effects such as: suicide attempt, suicidal thoughts and hostility (primarily aggressiveness, opposition and anger) when taking a medicine from this group. Nevertheless, the doctor may prescribe this medicine for patients under 18 years of age when he thinks it is for their benefit. Refer to the doctor again, if he prescribed this medicine for a patient under 18 years of age and you are interested in discussing it with him.
Inform the doctor if one or more of the symptoms listed above occurred or worsened in patients under 18 years of age taking the medicine. Additionally, there are no data regarding long-term safety effects of the medicine in regards to growth, maturation, and cognitive and behavioral development in this age group.
Tests and follow-up
Venla may cause undesirable effects that you will not be aware of, such as increased blood pressure or heart rate disturbances, mild changes in liver enzyme levels, sodium levels or blood cholesterol. More rarely, **Venla** may impair platelet activity and cause an increase in risk of bruises or bleeding. Therefore, the doctor may want to occasionally perform blood tests, especially if you are taking **Venla** for a prolonged period of time.
Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
Do not stop or start taking medicines, including non-prescription medicines or nutritional supplements, without first consulting the doctor.
Do not take monoamine oxidase inhibitors (MAOIs) used to treat depression or Parkinson's disease together with **Venla**. Tell the doctor if you have taken these types of medicines within the past 14 days. See detailed information in "Do not use the medicine if" section.
Serotonin syndrome:
A condition that may be life-threatening or neuroleptic malignant syndrome (NMS)-like symptoms (see section 4 "Side effects") may occur during the course of treatment with **Venla**. Especially when additional medicines are taken concomitantly.
Examples of these medicines include:
- triptans (for treating migraine).
- other medicines to treat depression, for example: selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors (SNRIs), tricyclic antidepressants or lithium-containing medicines.
- medicines that contain amphetamines (to treat attention deficit disturbances – ADHD, narcolepsy and obesity).
- medicines that contain linezolid, an antibiotic (to treat infections).
- medicines that contain moclobemide, a reversible monoamine oxidase inhibitor (MAOI) (to treat depression).
- medicines that contain sibutramine (for weight loss).
- medicines that contain tramadol (an analgesic), fentanyl, tapentadol, pethidine, or pentazocine (for relief of severe pains).
- medicines that contain dextromethorphan (for cough relief).
- medicines that contain methadone (to treat addiction to opiates or to treat severe pain).
- medicines that contain methylene blue (for treating high blood methemoglobin levels).
- preparations that contain St. John's Wort (also called Hypericum perforatum, an herbal extract used to treat mild depression).
- preparations that contain tryptophan (for sleep problems and as an antidepressant).
- antipsychotics (to treat a disease with symptoms such as hearing, seeing or feeling nonexistent things, delusions, paranoia, unclear thoughts, introversion).

Signs and symptoms of serotonin syndrome may include a combination of restlessness, hallucinations, lack of coordination, rapid heart rate, increased body temperature, rapid changes in blood pressure, increased reflexes, diarrhea, coma, nausea, vomiting.
Serotonin syndrome in its most severe form may resemble neuroleptic malignant syndrome (NMS). Signs and symptoms of this syndrome may include a combination of high fever, rapid heart rate, sweating, severe muscle rigidity, confusion, increased muscle enzymes (determined in blood tests).
Inform the doctor immediately, or proceed to the closest hospital emergency room, if you suspect that you are suffering from serotonin syndrome.
Tell the doctor if you are taking medicines that affect heart rate, such as:
- medicines to treat heart rate disturbances, such as: quinidine, amiodarone, sotalol or dofetilide
- antipsychotics, such as thioridazine (also see "Serotonin syndrome" above)
- antibiotics, such as erythromycin or moxifloxacin (to treat bacterial infections)
- antihistamines (to treat allergy)

The following medicines may react with **Venla**; therefore, use them with caution. It is especially important to inform the doctor or pharmacist if you are taking medicines that contain:
- atazanavir, clarithromycin, indinavir, itraconazole, voriconazole, posaconazole, ketoconazole, nelfinavir, ritonavir, saquinavir, telithromycin
- haloperidol or risperidone (to treat psychiatric conditions)
- metoprolol (beta blocker, to treat hypertension and heart problems)
- oral contraceptives

Taking Venla and food
Take **Venla** with food (see section 3 "How should you use the medicine?").
Use of the medicine and alcohol consumption
Avoid consuming alcohol while taking **Venla**.
Pregnancy, breastfeeding and fertility
If you are pregnant, or breastfeeding, think you are pregnant or are planning to become pregnant, consult the doctor before using this medicine. **Venla** can only be used after consulting the doctor regarding the possible benefit and the possible risks to the unborn baby.
Inform your doctor if you are using **Venla** during pregnancy.
When taken during pregnancy, similar medicines (SSRIs) may increase the risk for a severe condition in newborns called persistent pulmonary hypertension of the newborn (PPHN), which causes the newborn to breathe faster and to appear blueish. These symptoms usually appear within the first 24 hours after birth. If this happens to your baby, refer to a doctor immediately.
Another symptom that may appear in a newborn whose mother has taken **Venla** during pregnancy, is that the newborn does not feed properly, in addition to breathing problems . If your baby has these symptoms after the birth and you are concerned, contact the doctor for a consultation.
Venlafaxine passes into breast milk, and, therefore, there is a risk that the medicine will affect the baby. Therefore, consult with the doctor to decide whether you should stop breastfeeding or stop treatment with this medicine.
Driving and operating machinery
Do not drive or operate tools or machinery until you know how the medicine affects you.

Important information regarding some of the ingredients of the medicine
This medicine contains lactose. If you have been told in the past by the doctor that you have an intolerance to certain sugars, consult the doctor before starting treatment.
This medicine contains less than 1 millimole sodium (23 mg) per tablet, that is to say it is essentially "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE?
Always use the preparation 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 recommended dosage is generally 75 mg per day in divided doses. The doctor can decide to gradually increase the dosage, and, if necessary, up to a maximum dosage of 375 mg per day to treat depression.
If you are suffering from a liver or kidney disease, contact your doctor, as the doctor may change the dosage.
Do not exceed the recommended dosage.
Swallow the medicine with a little water.
Take the medicine with a meal, in the morning and evening, at around the same time every day.
If necessary, the tablet may be halved for immediate use. There is no information about crushing or chewing the tablet.
Use this medicine at specified time intervals, as determined by the attending doctor.
Do not stop taking the medicine, without consulting your doctor (See "If you stop taking the medicine" section).
If you accidentally take a higher dosage
If you took an overdose, refer to a doctor immediately.
If a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you. Symptoms of overdose can include rapid heart rate, changes in alertness (ranging from sleepiness to coma), blurred vision, seizures or convulsions and vomiting.
If you forget to take the medicine
If you forgot to take this medicine at the required time, take a dose as soon as you remember, but if it is time for the next dose, skip the forgotten dose and take the next dose as usual. Do not take a double dose to compensate for the forgotten dose. Never take more than the daily dose prescribed for you.
Adhere to the treatment regimen as recommended by the doctor.
If you stop taking the medicine
Even if there is an improvement in your health, do not stop treatment with the medicine or lower the dosage without consulting your doctor. Your doctor will tell you how to gradually lower the dosage before fully discontinuing the treatment if he thinks you no longer need to be treated with this medicine.
Sudden discontinuation of the medicine or too rapid a decrease in dosage, may be accompanied by side effects such as fatigue, dizziness, lightheadedness, headache, insomnia, nightmares, dry mouth, loss of appetite, nausea, diarrhea, nervousness, restlessness, confusion, ringing in the ears, tickling sensations, or, infrequently, sensations of electric shock, weakness, sweating, seizures, flu-like symptoms.
Your doctor will guide you as to how to gradually lower the dosage.
If you experience one or more of these symptoms, or other worrisome symptoms, consult your doctor.
Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS
As with any medicine, use of **Venla** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.
Discontinue use and refer to a doctor immediately or proceed to a hospital emergency room upon onset of one or more of the following side effects:
Uncommon side effects (effects occurring in 1-10 in 1,000 users):
Swelling of the face, mouth, tongue, throat, hands or feet and/or itchy, raised rash (urticaria), difficulty swallowing or breathing.
Rare side effects (effects occurring in 1-10 in 10,000 users):
- Chest tightness, wheezing, difficulty swallowing or breathing.
- Severe skin rash, itch or urticaria (raised red or colorless lesions on the skin, which are usually itchy).
- Signs and symptoms of serotonin syndrome that may include: restlessness, hallucinations, lack of coordination, rapid heart rate, increased body temperature, rapid changes in blood pressure, increased reflexes, diarrhea, coma, nausea, vomiting. Serotonin syndrome in its most severe form can resemble neuroleptic malignant syndrome (NMS). Signs and symptoms of this syndrome may include a combination of high fever, rapid heart rate, sweating, severe muscle rigidity, confusion, increased muscle enzymes (determined in a blood test).
- Signs of infection, such as high fever, chills, tremor, headaches, sweating and flu-like symptoms. These may be caused by a blood circulation disturbance that leads to increased risk of infections.
- Severe rash which may cause severe blisters and skin peeling.
- Unexplained muscle aches, tenderness or weakness. These may be signs of rhabdomyolysis.

Side effects of unknown frequency (effects whose frequency has not yet been determined):
- Suicidal thoughts and behavior (reported during treatment and close to discontinuation of venlafaxine treatment, see section 2 "Special warnings regarding use of the medicine").
- Signs and symptoms of a condition called "broken heart syndrome", which may include chest pain, shortness of breath, dizziness, fainting, irregular heart rate.

Other side effects that you should tell your doctor about include (the frequency of these side effects appears below, under "Additional side effects that may occur"):
- cough, wheezing and shortness of breath, that may be accompanied by high fever.
- black or bloody stools.
- itch, yellow skin or eyes, or dark urine, which may be symptoms of liver inflammation (hepatitis).
- heart problems, e.g., rapid or irregular heart rate, increased blood pressure.
- eye problems, e.g., blurred vision, dilated pupils.
- nerve problems, e.g., dizziness, sensation of pins and needles, movement difficulties (muscle spasms or stiffness), seizures or convulsions.
- psychiatric problems such as hyperactivity and feeling of euphoria (an exceptional feeling of overexcitement).
- withdrawal effects (see section 3 "How should you use the medicine?" in subsection "If you stop taking the medicine").
- prolonged bleeding – the bleeding may persist longer than usual if you were injured or got cut.

Additional side effects that may occur
Very common side effects (effects occurring in more than 1 user in 10):
- dizziness, headaches, sleepiness.
- insomnia.
- nausea, dry mouth, constipation.
- sweating (including night sweats).

Common side effects (effects occurring in 1-10 in 100 users):
- decreased appetite.
- confusion, feeling detached from yourself, inability to reach orgasm, decreased sex drive, restlessness, nervousness, abnormal dreams.
- tremor, restlessness or inability to sit or stand still, sensation of pins and needles, changes in sense of taste, increased muscle tone.
- visual disturbances, such as blurred vision, dilated pupils, inability of the eye to automatically switch focus from far to near objects.
- ringing in the ears (tinnitus).
- rapid heart rate, palpitations.
- increased blood pressure, flushing.
- shortness of breath, yawning.
- vomiting, diarrhea.
- mild rash, itch.
- increased frequency in urination, inability to pass urine and difficulty in passing urine.
- irregular menstruation, such as increased bleeding or increased irregular bleeding.
- an ejaculation/orgasm problem (in men), erection disturbances (impotence).
- weakness (asthenia), fatigue, chills.
- weight gain, weight loss.
- increased cholesterol levels.

Uncommon side effects (effects occurring in 1-10 in 1,000 users):
- hyperactivity, racing thoughts and reduced need to sleep (mania).
- hallucinations, feeling detached from reality, orgasm problems, lack of sensation or emotion, overexcitement, grinding of teeth.
- involuntary muscle movements, fainting, coordination and balance disturbances.
- Feeling dizzy (especially when rapidly standing up), reduced blood pressure.
- bloody vomit or black or bloody stools (may be a sign of internal bleeding).
- sensitivity upon exposure to the sun, bruises, abnormal hair loss.
- inability to control urination.
- muscle rigidity, spasms and involuntary movements.
- mild changes in blood liver enzyme level.

Rare side effects (effects occurring in 1-10 in 10,000 users):
- spasms or convulsions.
- cough, wheezing and shortness of breath that may be accompanied by high fever.
- disorientation and confusion, sometimes accompanied by hallucinations (delirium).
- increased water consumption (also called syndrome of inappropriate antidiuretic hormone secretion – SIADH).
- decrease in blood sodium levels.
- severe eye pain and deteriorated or blurred vision.
- abnormal, fast or irregular heart rate, which may lead to fainting.
- severe stomach pain or severe back pain (may indicate a severe intestinal, liver or pancreas problem).
- itch, yellow skin or yellow eyes, dark urine or flu-like symptoms – symptoms of liver inflammation (hepatitis).

Very rare side effects (effects occurring in less than 1 user in 10,000):
- prolonged bleeding – can be a sign of reduced platelet count – may lead to increased risk of bruises or bleeding.
- abnormal breast milk production.
- unexpected bleeding, such as bleeding of the gums, bloody urine or vomit, or unexpected onset of bruises or blood vessel injury (broken veins).

Side effects of unknown frequency (effects whose frequency has not yet been determined):
- aggressiveness.
- lightheadedness (vertigo).

If a side effect occurs, if one of the side effects worsens, or if you are suffering 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.
Additionally, you can report to "Unipharm Ltd.".

5. HOW SHOULD THE MEDICINE BE STORED?
- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the 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 at a temperature below 25°C and in a place protected from light.

6. FURTHER INFORMATION
In addition to the active ingredient, the medicine also contains:
Microcrystalline cellulose, lactose anhydrous, sodium starch glycolate, colloidal silicon dioxide, magnesium stearate, iron oxide red.
Each **Venla 37.5** tablet contains 30 mg lactose. Each **Venla 75** tablet contains 60 mg lactose.
What the medicine looks like and the contents of the package:
Venla is packaged in trays (blister) inserted into a carton package. Each package of **Venla** contains 7, 10, 14, 15, 28 or 30 tablets. Not all package sizes may be marketed.
Venla 37.5 and Venla 75 are round, biconvex, pink-spotted, film-coated tablets with a break line on one side.
Registration holder and address: Unipharm Ltd., P.O. Box 21429, Tel Aviv, 6121301.
Manufacturer and address: Unipharm Ltd., "Mevo Carmel" Industrial Park.
Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Venla 37.5: 129 98 30902 01
Venla 75: 129 99 30901 01
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