Patient package insert according to Pharmacists' Regulations (Preparations) – 1986

This medicine can be sold with a physician's prescription only

Viepax® 37.5, 75, Tablets

The medicine name and its strength:
Viepax 37.5: each tablet contains 37.5 mg Venlafaxine as the hydrochloride salt
Viepax 75: each tablet contains 75 mg Venlafaxine as the hydrochloride salt

Inactive and allergic ingredients, contained in the medicine: see section 6 "Additional information" and "Important information about some of the ingredients of the medicine" in section 2.

Read the entire leaflet carefully before you start using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.

Antidepressants and medicines used to treat anxiety increase the risk of suicidal thoughts and behavior in children, adolescents and young adults up to age 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 etc. If changes like these occur, refer to the doctor immediately (see section 2).

1. What is the medicine intended for?

Viepax is intended for treatment of depression.
Therapeutic group: Venlafaxine is an antidepressant, which belongs to a group of medicines called serotonin-norepinephrine reuptake inhibitors (SNRIs). This group of medicines is used to treat depression and other conditions such as anxiety. . The mechanism of action of antidepressants is not clear enough, however the medicines may affect by increasing the levels of serotonin and norepinephrine in the brain. Treating depression appropriately is important in order to improve your condition. Without treatment, your condition may not pass and may even worsen, thus it will be hard to treat in the future.

2. Before using the medicine

Do not use the medicine if:

- you are hypersensitive (allergic) to the active ingredient (venlafaxine) or any of the other ingredients the medicine contains (see section 6).
- you are taking or have taken monoamine oxidase enzyme irreversible inhibitors (MAOIs), used for treatment of depression and Parkinson's disease in the last 14 days. Taking irreversible MAOI type medicines together with **Viepax** may cause severe and life-threatening side effects. In addition, you should wait at least 7 days since ending treatment with **Viepax** until starting treatment with MAOI. See section "Drug interactions" and information in this section regarding "serotonin syndrome".

Special warnings regarding the use of this medicine

- **Before treatment with Viepax, tell the doctor if:**
  - you are taking additional medicines that increase the risk of serotonin syndrome , a potentially life-threatening condition, when taken together with **Viepax** (see section "Drug interactions").
  - you suffer from eye problems, such as certain types of glaucoma (increased intraocular pressure).
  - you have previously suffered from hypertension.
  - you have previously suffered from cardiac problems.
  - you have been told that you suffer from irregular heartbeat.
  - you have previously suffered from convulsions (seizures).
  - you have previously suffered from low blood sodium levels (hyponatremia).
  - you have a history of bleeding problems (a tendency to develop bruises [subcutaneous hemorrhages] or to bleed easily), or if you are taking medicines that might increase the risk of bleeding, such as warfarin (used to prevent blood clots), or if you are pregnant (see "Pregnancy breastfeeding and fertility" in section 2).
  - you or your family member have previously suffered from mania or bipolar disorder (feeling over-excited or euphoric).
  - you have a history of aggressive behavior.
- **Viepax** may cause a sense of restlessness or inability to sit or stand still during the first weeks of treatment. Tell the doctor if you suffer from this condition.
- Do not drink alcohol while being treated with **Viepax** as it can lead to extreme tiredness and unconsciousness. Concomitant use of **Viepax** with alcohol and/or certain medicines can make your symptoms of depression and other conditions, such as anxiety disorders worse.
- Suicidal thoughts and worsening of your depression or anxiety disorder:
  If you are depressed and/or suffer from anxiety disorder, you may have thoughts of harming yourself or suicidal thoughts. These thoughts may worsen when you first start taking antidepressants, since it takes time for these medicines to start acting, usually about two weeks, but sometimes longer. These thoughts may also occur when the dose of the medicine is decreased or during discontinuation of treatment with **Viepax**.
  You may be more likely to have these thoughts if:
  - you have previously had suicidal thoughts or thoughts of harming yourself.
  - you are a young adult. Information from clinical trials has shown that an increased risk of suicidal behavior exists in young adults (under the age of 25) with psychiatric conditions, who were treated with antidepressants.

  If you have thoughts of harming yourself or suicidal thoughts at any time, contact your doctor or refer immediately to a hospital emergency room.
  It may be useful to tell a relative or a friend if you suffer from depression or anxiety disorder and ask them to read this leaflet. Ask them if, in their opinion, your depression or anxiety is getting worse, 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 tooth decay, and therefore care should be taken with dental hygiene.
- Diabetes: Blood sugar levels may change due to treatment with **Viepax**, therefore, if you are diabetic, consult the doctor regarding dose adjustment of diabetes medicines.
- Sexual dysfunction: medicines such as venlafaxine (called serotonin-noradrenaline reuptake inhibitors [SNRIs]) may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms lasted after stopping the treatment.

Children and adolescents

This medicine is not recommended for use in children and adolescents under 18 years of age. You should also know that patients under 18 years of age are at a higher risk of side effects such as suicide attempts, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when taking a medicine from this group. Despite this, the doctor may prescribe this medicine for patients under 18 years of age when he thinks that it is in their best interest. If the doctor has prescribed the medicine to a patient under 18 years of age and you wish to discuss this with the doctor - refer back to him.
Inform the doctor if any of the symptoms listed above, appeared or got worse in patients under 18 years of age taking the medicine.
Also, there is no data, regarding long-term safety effects of the medicine concerning growth, maturation and cognitive and behavioral development in this age group.

Tests and follow up

Viepax may sometimes cause unwanted effects that you may not be aware of, such as rise in blood pressure, heart rate disturbance, mild changes in blood levels of liver enzymes, sodium or cholesterol. More rarely, **Viepax** can impair blood platelets function and cause an increase in the risk of bruising or bleeding. Therefore, the doctor may request to perform occasional blood tests, particularly if you have been taking **Viepax** for a prolonged period.

Drug interactions

If you are taking or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Your doctor should decide whether you can take Viepax with other medicines. Do not start or stop taking medicines, including non-prescription medicines and nutritional supplements without first consulting the doctor.

- **Monoamine oxidase inhibitors (MAOIs)**, which are used to treat depression or Parkinson's disease, must not be taken concomitantly with **Viepax**. Tell the doctor if you have taken this type of medicines within the last 14 days. See detailed information in section "Do not use the medicine if" under this section.
  Serotonin syndrome:
  A potentially life-threatening condition or neuroleptic malignant syndrome (NMS)-like symptoms (see section 4 "Side Effects") may occur during treatment with venlafaxine, particularly when other medicines are taken concomitantly.
  Examples of these medicines include:
  - Triptans (for treating migraine)
  - Other medicines for treatment of depression, such as: selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs), tricyclic antidepressants or medicines containing lithium
  - Medicines containing amphetamines (for treating attention deficit hyperactivity disorder - ADHD, narcolepsy and obesity)
  - Medicines containing linezolid, an antibiotic (for treating infections)
  - Medicines containing moclobemide, a MAO inhibitor (for treating depression)
  - Medicines containing sibutramine (for weight loss)
  - Medicines containing opioids [e.g., tramadol (analgesic), fentanyl, tapentadol, pethidine, pentazocine, buprenorphine (for relieving severe pain), buprenorphine/naloxone (for treating opiate dependence)]
  - Medicines containing dextromethorphan (for cough relief)
  - Medicines containing methadone (for treating addiction to opioids or for treating severe pain)
  - Medicines containing methylene blue (for treating high levels of methaemoglobin in the blood)

- Products containing St. John's Wort (also called hypericum perforatum, a herbal remedy used to treat mild depression)
- Products containing tryptophan (for sleep and depression problems)
- Antipsychotic medicines (for treating a disease with symptoms such as: hearing, seeing or sensing nonexistent things, false beliefs, unusual suspiciousness, unclear rationality, becoming withdrawn)

Signs and symptoms of serotonin syndrome may include a combination of: involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, excessive sweating, tremor, increased muscle tension, restlessness, hallucinations, loss of coordination, fast heartbeat, body temperature above 38°C, fast changes in blood pressure, increased reflexes, diarrhea, coma, nausea, vomiting. Contact your doctor when experiencing such symptoms. In its most severe form, serotonin syndrome can resemble neuroleptic malignant syndrome (NMS). Signs and symptoms of this syndrome may include a combination of high fever, fast heart rate, sweating, severe muscle stiffness, confusion, muscle enzymes increase (determined by a blood test).
Notify the doctor immediately or refer to an emergency room of the nearest hospital if you think you have serotonin syndrome.

Inform the doctor if you are taking medicines that affect heart rate, for example:
- Antiarrhythmics such as: quinidine, amiodarone, sotalol or dofetilide
- Antipsychotic medicines such as thioridazine (see also "Serotonin syndrome" above)
- Antibiotics, such as erythromycin or moxifloxacin (for treating bacterial infection)
- Antihistamines (for treating allergy)

The following medicines may interact with **Viepax**, therefore, they should be used with caution. It is particularly important to inform the doctor or the pharmacist if you are taking medicines containing:
- Ketoconazole (an antifungal medicine)
- Haloperidol or risperidone (for treating psychiatric conditions)
- Metoprolol (a beta blocker, for treating high blood pressure and cardiac problems)
- Oral contraceptives.

Use of the medicine and food
Take **Viepax** with food (see section 3 "How to use this medicine").

Use of the medicine and alcohol consumption
Do not drink alcohol while being treated with **Viepax**. Concomitant use with alcohol can lead to extreme tiredness and unconsciousness and can make your symptoms of depression and other conditions, such as anxiety disorders worse.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you are pregnant or planning to become pregnant, consult the doctor before using this medicine. **Viepax** can be used only after consulting the doctor about potential benefit and possible risks to the fetus. Inform the doctor if you are taking **Viepax** during pregnancy.
While taken during pregnancy, similar medicines (SSRIs) may increase the risk for a dangerous condition in babies, called persistent pulmonary hypertension of the newborn (PPHN), which causes the newborn to breathe more rapidly and look bluish. These symptoms usually appear during the first 24 hours after the baby was born. If this happens to your baby, refer to your doctor immediately.

If you take **Viepax** 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. Your doctor or midwife should be aware that you are taking **Viepax** so they can advise you.
If you are taking **Viepax** during pregnancy, in addition to breathing problems, an additional symptom that may appear is that the newborn does not eat properly. If your baby has these symptoms after birth and you are concerned, contact the doctor for consultation.
Venlafaxine passes into breast milk, therefore there is a risk that the medicine will affect the baby. Hence, consult the doctor in order to decide whether you should stop breastfeeding or stop treatment with this medicine.

Driving and use of machines
Do not drive a car or operate tools or machines until you know how the medicine affects you.

Important information about some of the ingredients of the medicine
Viepax contains lactose. If you have previously been told by a doctor that you have intolerance to certain sugars, consult the doctor before starting treatment.
This medicine contains less than 1 millimole sodium (23 mg) per tablet, hence it is actually 'sodium free'.

3. How to use this medicine
Always use the medicine as instructed by the doctor. You should check with your doctor or pharmacist if you are not sure.
Dosage and treatment regimen will be determined exclusively by the doctor. The usual dosage is 75 mg per day in divided doses. The doctor can decide to increase the dosage gradually and if necessary, up to a maximum daily dosage of 375 mg for treating depression.
Do not exceed the recommended dosage.
Take the medicine in the morning and in the evening, at about the same times every day. Take the medicine with a meal. Do not halve the tablet, due to a lack of score line. There is no information regarding crushing/chewing.
If you suffer from liver or kidney problems, tell your doctor, since it may be required to change the dosage of this medicine.
Do not stop taking this medicine without consulting your doctor (see section "If you stop taking the medicine").

If you have accidently taken a higher dosage
If you have taken an overdose, refer immediately to the doctor.
If a child has accidentally swallowed the medicine, refer immediately to the doctor or to a hospital emergency room. Bring the package of the medicine with you.
Overdose can be life-threatening, especially with concomitant use of alcohol and/or certain medicines (see in section 2 "Drug interactions").
Symptoms of overdose may include: rapid heartbeat, changes in level of alertness (ranging from sleepiness to coma), blurred vision, seizures or spasms and vomiting.

If you forgot to take the medicine
If you forgot to take the medicine at the intended time, take a dose as soon as you remember. However, if it is time for a next dose, skip the forgotten dose and take the next dose as usual. Do not take a double dose to make up for a forgotten dose. By no means, do not take more than your daily prescribed dose.
Continue with the treatment as recommended by the doctor.

If you stop taking the medicine

Do not stop treatment with the medicine or reduce the dosage without consulting your doctor, even if there is an improvement in your health condition. If the doctor thinks that you no longer need treatment with the medicine, he will instruct you how to reduce the dosage gradually before completely stopping treatment. Ceasing treatment suddenly or reducing dosage too quickly may be accompanied by side effects such as: suicidal thoughts, aggressiveness, tiredness, dizziness, spinning sensation, headache, insomnia, nightmares, dry mouth, loss of appetite, nausea, diarrhea, nervousness, restlessness, confusion, ringing in the ears, tingling or, rarely, electric shock sensations, weakness, sweating, seizures or flu-like symptoms, problems with eyesight and increase in blood pressure (which can cause headache, dizziness, ringing in the ears, sweating, etc.).
Your doctor will advise you on how you should gradually discontinue **Viepax** treatment. This can take a period of several weeks or months. In some patients, discontinuation may need to occur very gradually over periods of months or longer. If you experience any of these symptoms or other concerning symptoms, consult your doctor.
Do not take medicines in the dark! Check the label and dose each time you take a medicine. Wear glasses if you need them.
If you have any further questions regarding the use of this medicine, consult a doctor or pharmacist.

4. Side effects

Like any medicine, the use of **Viepax** may cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.

Stop use and refer immediately to the doctor or a hospital emergency room with the appearance of one or more of the following side effects:

Uncommon side effects (effects that appear in 1-10 users out of 1,000):

- Swelling of the face, mouth, tongue, throat, hands or feet and/or an itchy protrusive rash (hives), swallowing or breathing difficulties.

Rare side effects (effects that appear in 1-10 users out of 10,000):

- Chest tightness, wheezing, swallowing or breathing difficulties.
- Severe skin rash, itching or hives (elevated patches of red or colorless skin that often itch).
- Signs and symptoms of serotonin syndrome which may include: restlessness, hallucinations, lack of coordination, fast heartbeat, rise in body temperature, fast changes in blood pressure, increased reflexes, diarrhea, coma, nausea, vomiting. In its most severe form, serotonin syndrome can resemble neuroleptic malignant syndrome (NMS). Signs and symptoms of this syndrome may include a combination of high fever, fast heartbeat, sweating, severe muscle stiffness, confusion, increase in muscle enzymes (determined by a blood test).
- Signs of an infection such as high fever, shivers, shaking, headaches, sweating and flu-like symptoms. These may be derived from a blood system impairment, which leads to an increased risk for infections.
- Severe rash, which may cause severe blisters and peeling of the skin.
- Unexplained muscle pain, sensitivity or weakness. These may be signs of muscle breakdown (rhabdomyolysis).

Side effects with unknown frequency (effects whose frequency has yet to be determined):

- Suicidal thoughts and suicidal behavior (reported during treatment and in conjunction with ceasing treatment with venlafaxine, see section 2 "Special warnings regarding the use of this medicine").
- Signs and symptoms of a condition called "broken heart syndrome" which may include chest pain, dyspnea, dizziness, fainting, irregular heartbeat.

Other side effects, **which you should tell your doctor about** include (the frequency of these side effects appears below under "Additional side effects that may occur"):
- Coughing, wheezing and shortness of breath which may be accompanied by high fever
- Melena or blood in the stool
- Itchiness, yellow skin or yellow eyes, or dark urine, which may be symptoms of a liver infection (hepatitis)
- Cardiac problems such as fast or irregular heart rate, high blood pressure
- Eye problems such as blurred vision, dilated pupils
- Neural problems such as dizziness, pins and needles sensation, movement difficulty (muscle contraction or stiffness), seizures or spasms
- Psychiatric problems such as hyperactivity and an unusual feeling of overexcitement
- Withdrawal effects (see section 3 "How to use this medicine", "If you stop taking the medicine")
- Prolonged bleeding - the bleeding may last longer than usual if you have been injured or cut

Additional side effects that may occur:

Very common side effects (effects that appear in more than 1 user out of 10):
- Dizziness, headaches, drowsiness
- Insomnia
- Nausea, dry mouth, constipation
- Sweating (including night sweats)

Common side effects (effects that appear in 1-10 users out of 100):
- Decreased appetite
- Confusion, feeling detached from yourself, lack of sexual satisfaction, decreased libido, restlessness, nervousness, abnormal dreams
- Tremor, restlessness or inability to sit or stand still, pins and needles sensation, altered sense of taste, increased muscle tension
- Visual disturbances including blurred vision, dilated pupils, inability of the eye to automatically change focus from distant to near objects
- Ringing in the ears (tinnitus)
- Rapid heart rate, feeling palpitations
- Blood pressure increase, flushing
- Shortness of breath, yawning
- Vomiting, diarrhea
- Mild rash, itchiness
- Increased frequency of urination, inability to urinate, urination difficulty
- Irregular menstruation such as increased bleeding or increased irregular bleeding; ejaculating/reaching sexual satisfaction problems (in men); erectile dysfunction (impotence)
- Weakness (asthenia), fatigue, chills
- Weight gain, weight loss
- Increase in cholesterol levels

Uncommon side effects (effects that appear in 1-10 users out of 1,000):

- Over activity, running thoughts and decreased need for sleep (mania)
- Hallucinations, feeling detachment from reality, problems reaching sexual satisfaction, lack of sensation or emotion, feeling overexcited, grinding of the teeth
- Fainting, involuntary muscular movements, impaired coordination and balance
- Feeling of dizziness (particularly in a quick transition to standing up), blood pressure decrease
- Vomiting blood or melena or bloody stool (may be a sign of internal bleeding)
- Sensitivity in exposure to sunlight, bruises, abnormal hair loss
- Inability to control urination
- Stiffness, contractions and involuntary muscular movements
- Mild changes in blood levels of liver enzymes

Rare side effects (effects that appear in 1-10 users out of 10,000):

- Seizures or spasms
- Coughing, wheezing and shortness of breath which may be accompanied by high fever
- Disorientation and confusion, often accompanied by hallucinations (delirium)
- Increased water consumption (also called syndrome of inappropriate antidiuretic hormone – SIADH)
- Decrease in blood sodium levels
- Severe eye pain and decreased or blurred vision
- Abnormal heart rate, rapid or irregular, that may lead to fainting
- Severe abdominal or back pain (may indicate a severe problem in the intestine, liver or pancreas)
- Itchiness, yellow skin or yellow eyes, dark urine or flu-like symptoms - symptoms of a liver inflammation (hepatitis)

Very rare side effects (effects that appear in less than 1 user out of 10,000):

- Prolonged bleeding, may be a sign of reduced number of platelets - may lead to an increase in the risk of bruising or bleeding
- Abnormal breast milk production
- Unexpected bleeding e.g. gum bleeding, blood in urine or vomit, or unexpected appearance of bruises or damage to blood vessels (broken veins)

Side effects with unknown frequency (effects, whose frequency has yet to be determined):

- Aggression
- Spinning sensation (vertigo)
- Heavy vaginal bleeding shortly after birth (postpartum hemorrhage), see "Pregnancy breastfeeding and fertility" in section 2 for further information

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

Side effects can be reported to the Ministry of Health by clicking on the link "דיווח על תופעות לוואי עקב טיפול תרופתי" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine, and any other medicine, must be stored 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 the medicine after the expiry date (תאריך תפוגה) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions**: store in a dry place, below 25°C.
- Medicines should not be disposed of via sewer or household waste. Ask your pharmacist how to dispose of medicines no longer in use. These measures will help to protect the environment.

6. Additional information

In addition to the active ingredient, the medicine also contains:
Lactose monohydrate, cellulose microcrystalline, sodium starch glycolate, povidone, magnesium stearate, ferric oxide yellow, ferric oxide brown.

What the medicine looks like and what the package contains:
Viepax 37.5: Beige round tablets.
Viepax 75: Beige round tablets.
Approved package sizes: 10, 14, 28, 30 tablets.
Not all package sizes may be marketed.

Registration number of the medicine at national drug registry of the Ministry of Health:
Viepax 37.5: 130683101500.
Viepax 75: 130693101600.

Revised in April 2023 according to MoH guidelines.

Manufacturer and registration holder: Dexcel Ltd. 1 Dexcel St., Or Akiva 3060000, Israel