Patient package insert according to Pharmacists' Regulations (Preparations) – 1986
This medicine can be sold with a physician's prescription only

VIEPAX® XR 75, PROLONGED RELEASE CAPLETS
VIEPAX® XR 150, VIEPAX® XR 225, PROLONGED RELEASE TABLETS

Viepax XR 75: each prolonged release caplet contains Venlafaxine (as hydrochloride) 75 mg
Viepax XR 150, Viepax XR 225: each prolonged release tablet contains Venlafaxine (as hydrochloride) 150 or 225 mg respectively

Inactive ingredients and allergens in the medicine - see section 6 "Additional information".

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

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.
Upon initiation of treatment with the medicine, patients of all ages, and their relatives, must monitor behavioral changes, such as worsening of depression, suicidal thoughts, aggression and the like.
If such changes occur, refer to a doctor immediately (see section 2).

1. What is the medicine intended for?

Viepax XR is intended for treatment of patients suffering from depression as well as for maintenance therapy of recurrent depression.
It is also for treatment of patients with the following anxiety disorders: generalized anxiety and social anxiety.

Therapeutic group: Venlafaxine belongs to a group of medicines called serotonin and norepinephrine reuptake inhibitors (SNRIs).
This group of medicines is used to treat depression and other conditions such as various anxiety disorders. The mode of action of antidepressants is not fully understood, but the medicines can have an affect by increasing the levels of serotonin and norepinephrine in the brain.
Treating depression and anxiety disorders is very important. Without treatment, your condition may not resolve and may even worsen, so that it will be more difficult 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 to any of the other ingredients this medicine contains (see section 6).
- You are taking or have taken medicines to treat depression or Parkinson's disease belonging to the monoamine oxidase inhibitors class (MAOIs). Taking MAOI-type medicines with **Viepax XR** may cause severe and life-threatening side effects. Wait 14 days from the day of finishing treatment with an MAOI until starting treatment with **Viepax XR**, and at least 7 days after finishing treatment with **Viepax XR** before starting treatment

with an MAOI. See section "Drug interactions" and information in this section regarding "Serotonin syndrome".

Special warnings regarding the use of the medicine
Before the treatment with Viepax XR, tell the doctor if:

- you are taking additional medicines that increase the risk of developing serotonin syndrome when taken together with **Viepax XR** (see section "Drug interactions")
- you are suffering from eye diseases such as certain kinds of glaucoma (increased pressure in the eye)
- you have suffered in the past from high blood pressure
- you have suffered in the past from heart diseases
- you have been told that you suffer from abnormal or fast heart rhythm
- you have suffered in the past from fits (seizures)
- you have suffered in the past from low blood sodium levels (hyponatremia)
- you have suffered in the past from bleeding disorders (a tendency to develop bruises [hemorrhaging under the skin] or a tendency to bleed easily), or if you are taking medicines that may increase the risk of bleeding such as warfarin (to prevent blood clotting), or if you are pregnant (see section "Pregnancy and breastfeeding")
- you have suffered in the past from, or if someone in your family has suffered, mania or bipolar disorder (manic depression)
- you have a history of aggressive behavior
- you are pregnant, planning to become pregnant or to breastfeed (see section "Pregnancy and breastfeeding")

Viepax XR may cause a sensation of restlessness or an inability to sit or stand still during the first few weeks of treatment. Tell the doctor if you suffer from this condition.
Do not drink alcohol while being treated with **Viepax XR** as it can lead to extreme tiredness and unconsciousness. Concomitant use with alcohol and/or certain medicines can make your symptoms of depression and other conditions such as anxiety disorders worse.

Viepax XR may not start to work immediately. Some people taking antidepressants may feel worse before feeling better. Your doctor may ask to see you again in a couple of weeks after you start treatment and then regularly until you start to feel well again. Tell your doctor if you do not start to feel better.

<u>Suicidal thoughts and worsening of your depression or anxiety disorder:</u>
If you are depressed and/or suffering from an anxiety disorder, you may have thoughts of harming yourself or suicidal thoughts. These thoughts may worsen when you start using antidepressants, since these medicines take time to start working, usually about two weeks, but sometimes longer. These thoughts may also occur when the dosage of the medicine is decreased or during discontinuation of treatment with the medicine.
You may be more likely to think like this if:

- you had in the past suicidal thoughts or thoughts of harming yourself.
- you are a young adult. Data from clinical studies have shown that there is an increased risk of suicidal behavior in young adults (below the age of 25) with psychiatric conditions that were treated with antidepressants.

If you have thoughts of harming yourself or suicidal thoughts at any time, contact your doctor or proceed immediately to a hospital emergency room.

It is recommended to tell a relative or a friend if you suffer from depression or an anxiety disorder, and ask them to read this leaflet. Ask them if in their opinion your depression or anxiety has gotten worse, or if they are worried 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. Therefore, you should take special care in your oral hygiene.

Diabetes
The level of blood sugar may change due to treatment with **Viepax XR,** therefore, if you are diabetic, consult with the doctor about adjusting the dosage of your diabetes medicines.

Sexual dysfunction
Medicines like **Viepax XR**, so-called serotonin and norepinephrine reuptake inhibitors (SNRIs), may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms continue after stopping treatment. See section 4 "Side effects" for further information.

If you feel restless, unable to stand still, feel "high" or very over-excited, or if you have jerky muscle movements which you cannot control, refer to a doctor immediately. See section 4 "Side effects" for further information.

Use in children and adolescents under the age of 18
This medicine is not recommended for use in children and adolescents under the age of 18. Also, you should know that children and adolescents under the age of 18 have an increased risk of side effects, such as attempted suicide, suicidal thoughts and hostility (predominantly aggression, oppositional behavior and anger), when taking this type of medicine.
Despite this, the doctor can prescribe this medicine to patients under the age of 18 if he thinks it is in their best interest. If the doctor has prescribed the medicine to a patient under the age of 18 and you want to consult with the doctor about it – refer back to him. Inform your doctor if one or more of the symptoms listed above have appeared or worsened in patients under the age of 18 taking the medicine. Additionally, there is 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
Viepax XR may sometimes cause undesirable side effects that you will not be aware of, such as increased blood pressure or abnormal heart rhythm, slight changes in liver enzyme levels, sodium or cholesterol levels in the blood. More infrequently, **Viepax XR** may impair platelet activity and cause an increase in risk of bruises or bleeding. Therefore, the doctor may occasionally ask to perform blood tests, especially if you are taking **Viepax XR** for a long period of time.

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. Do not stop or start taking any medicines, including non-prescription medicines and nutritional supplements without first consulting the doctor. The doctor will decide whether you can take Viepax XR with other medicines.

- **Do not take monoamine oxidase inhibitors (MAOIs)** which are used to treat depression or Parkinson's disease, together with **Viepax XR**. Tell the doctor if you have taken medicines of this type within the last 14 days. See detailed information in section "Do not use the medicine if", in this section.
- **Serotonin syndrome:**
  A condition that may be life-threatening or neuroleptic malignant syndrome (NMS)-like symptoms (see section 4 "Side effects") can occur during treatment with venlafaxine, especially when taken concomitantly with other medicines.
  Examples of such medicines include:
  - Triptans (for treating migraine)
  - Other medicines for the treatment of depression, for instance: selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants or lithium-containing medicines
  - Medicines containing:
    - Amphetamines (to treat attention deficit hyperactivity disorder - ADHD, narcolepsy and obesity)
    - Linezolid, an antibiotic (for treatment of infections)
    - Moclobemide, a type of monoamine oxidase inhibitor (MAOI) (for treatment of depression)
    - Sibutramine (for weight loss)
    - Opioids (e.g., buprenorphine, tramadol, fentanyl, tapentadol, pethidine or pentazocine for treatment of severe pain)
    - Dextromethorphan (to alleviate cough)
    - Methadone (for treatment of addiction to opiates or to treat severe pain)
    - Methylene blue (for treatment of high levels of methemoglobin in the blood)
  - Preparations containing St. John's Wort (also called Hypericum perforatum, a plant extract used for treatment of mild depression)
  - Preparations containing tryptophan (for sleep problems and depression)
  - Antipsychotic medicines (to treat a disease with symptoms, such as hearing, seeing or sensing things which do not exist, mistaken beliefs, unusual suspiciousness, unclear reasoning, becoming withdrawn).

Signs and symptoms of serotonin syndrome may include a combination of restlessness, hallucinations, lack of coordination, fast heartbeat, increased body temperature, fast changes in blood pressure, overactive 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, fast heartbeat, sweating, severe muscle stiffness, confusion, increased muscle enzymes (determined by a blood test).

Tell the doctor immediately or proceed to the emergency room at the nearest hospital, if you think you have serotonin syndrome.
Inform the doctor if you are taking medicines that affect heart rhythm, for example:
- Medicines to treat heart rhythm disturbances, such as quinidine, amiodarone, sotalol or dofetilide
- Antipsychotics such as thioridazine (see also "Serotonin syndrome" above)
- Antibiotics, such as erythromycin or moxifloxacin (to treat bacterial infection)
- Antihistamines (to treat allergy)

The following medicines may interact with **Viepax XR** and should therefore be used with caution. It is particularly important to inform the doctor or pharmacist if you are taking medicines containing:
- Ketoconazole (an antifungal medicine)
- Haloperidol or risperidone (to treat psychiatric conditions)
- Metoprolol (a beta blocker, to treat hypertension and heart problems)

Use of the medicine and food
Viepax XR should be taken with food (see section 3 "How to use the medicine").

Use of the medicine and alcohol consumption
Avoid alcohol consumption while you are taking **Viepax XR**.

Do not drink alcohol while being treated with **Viepax XR** as it can lead to extreme tiredness and unconsciousness. Concomitant use with alcohol and/or certain medicines can make your symptoms of depression and other conditions such as anxiety disorders worse.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you are pregnant or plan to become pregnant, consult your doctor before using this medicine.
Viepax XR can only be used after discussing the potential benefit and the potential risks to the fetus with the doctor.

Inform the doctor that you are taking **Viepax XR** during the pregnancy.
When taken during pregnancy, similar medicines (selective serotonin reuptake inhibitors SSRIs) may increase the risk of persistent pulmonary hypertension of the newborn (PPHN), a condition that makes the newborn breathe faster and appear bluish. These symptoms usually appear during the first 24 hours after the baby is born. If this happens to your baby, refer to your doctor immediately.

If you take **Viepax XR** 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 the doctor that you are taking **Viepax XR**.

Another symptom that may appear in the newborn whose mother took **Viepax XR** during pregnancy, is that the newborn may not feed properly. If your baby has these symptoms after birth and you are concerned, contact the doctor.

Viepax XR 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 using machines
Do not drive a car or operate machinery until you know how the medicine affects you.

3. How to use the medicine?
Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.
The dosage and manner of treatment will be determined by the doctor only.

The usual recommended starting dosage is 75 mg per day. The doctor may increase the dosage, if needed.

Do not exceed the recommended dose.

Method of administration
The medicine should be taken with food, at approximately the same time each day, either in the morning or in the evening. The medicine should be swallowed whole with water.
Do not crush/divide/chew/dissolve the medicine, to avoid compromising the extended release of the medicine.

Tell your doctor if you suffer from liver or kidney problems, since the dosage of the medicine may be different.
Do not stop taking the medicine without consulting the doctor. A sudden discontinuation may lead to withdrawal symptoms (see also section "If you stop taking the medicine").

If you have accidentally taken a higher dosage
If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

Overdose can be life-threatening, especially with concomitant use of alcohol and/or certain medicines (see “Drug interactions” in section 2).
The symptoms of an overdose may include a rapid heartbeat, changes in the level of alertness (ranging from sleepiness to coma), blurred vision, seizures or fits and vomiting.

If you forgot to take the medicine
If you forgot to take this medicine at the designated time, take a dose as soon as you remember. However, if it is time for the next dose, skip the forgotten dose and take the next dose as usual. Under no circumstances should two doses be taken together to make up for the forgotten dose! Do not take more than the daily dose prescribed for you.

Continue with the treatment 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 reduce the dosage without consulting the doctor. The doctor will instruct you on how to gradually reduce the dosage before stopping treatment completely if he thinks that you no longer need to be treated with this medicine.
Sudden discontinuation of taking the medicine or a reduction in dosage too rapidly may be accompanied by side effects, such as suicidal thoughts, aggressiveness, tiredness, dizziness, light-headedness, tremor, headache, insomnia, nightmares, dry mouth, decreased appetite, nausea, vomiting, diarrhea, nervousness, agitation, confusion, ringing in the ears, tingling sensation 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.).

The doctor will instruct you on how you should gradually discontinue the treatment with the medicine. 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 the doctor.

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 on the use of this medicine, consult the doctor or pharmacist.

4. <u>Side effects</u>

Like any medicine, the use of **Viepax XR** 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.

Stop taking this medicine and refer to the doctor or to a hospital emergency room immediately with the occurrence of one or more of the following side effects:

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):
- Swelling of the face, tongue, mouth, throat, hands or feet and/or itchy and raised rash (hives), difficulty swallowing or breathing

Rare side effects (effects that occur in 1-10 out of 10,000 users):
- Chest tightness, wheezing, difficulty swallowing or breathing
- Severe skin rash, itching or hives (elevated, red or colorless skin patches that usually itch)
- Signs and symptoms of serotonin syndrome which may include: restlessness, hallucinations, lack of coordination, fast heartbeat, increased body temperature, fast changes in blood pressure, overactive 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, fast heartbeat, sweating, severe muscle stiffness, confusion, increased muscle enzymes (determined by a blood test)
- Signs of infection, such as high fever, chills, shivering, headaches, sweating and flu-like symptoms. These may be caused by a blood system disturbance, which leads to increased risk of infections
- Severe rash which may cause severe blistering and peeling of the skin
- Unexplained muscle pain, tenderness or weakness. These may be signs of muscle breakdown (rhabdomyolysis)

Side effects with unknown frequency (effects for which a frequency has not yet been determined):
- Signs and symptoms of a condition called "broken heart syndrome" (stress cardiomyopathy or takotsubo cardiomyopathy) which may include chest pain, shortness of breath, dizziness, fainting, irregular heartbeat.

Other side effects **that you must tell your doctor about** include (the frequency of these side effects is indicated below under "Additional side effects that may occur"):
- Coughing, wheezing and shortness of breath, that may be accompanied by a high fever
- Black stools or blood in stools
- Itching, yellow skin or eyes, or dark urine, which may be symptoms of liver inflammation (hepatitis)
- Heart problems, such as rapid or irregular heartbeat, increased blood pressure
- Eye problems, such as blurred vision, dilated pupils

- Neural problems, such as dizziness, pins and needles, movement difficulty (muscle spasms or stiffness), seizures or fits
- Psychiatric problems, such as hyperactivity and feeling unusually overexcited
- Withdrawal effects (see "How to use the medicine?", "If you stop taking the medicine" in section 3)
- Prolonged bleeding - the bleeding may continue for longer than usual if you were injured or got cut

Additional side effects that may occur:
Very common side effects (effects that occur in more than 1 in 10 users):
- Dizziness, headaches, drowsiness, insomnia
- Nausea, dry mouth, constipation
- Sweating (including night sweats)

Common side effects (effects that occur in 1-10 out of 100 users):
- Decreased appetite
- Confusion, feeling of detachment from yourself, lack of orgasm, decreased libido, agitation, nervousness, abnormal dreams
- Tremor, restless feeling or inability to sit or stand still, sensation of pins and needles, changes in sense of taste, increased muscle tension
- Visual disturbances including blurred vision, dilated pupils, inability of the eye to change focus from distant to near objects
- Ringing in the ears (tinnitus)
- Rapid heartbeat, palpitations, increase in blood pressure, flushing
- Shortness of breath, yawning
- Vomiting, diarrhea
- Mild rash, itching
- Increased frequency of urination, inability to pass urine, difficulty in passing urine
- Menstrual irregularities (in women), such as increased bleeding or increased irregular bleeding, ejaculation/reaching an orgasm problems (in men), erectile dysfunction (impotence)
- Weakness, fatigue, chills
- Weight gain, weight loss, increased cholesterol levels

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):
- Hyperactivity, racing thoughts and reduced need to sleep (mania)
- Hallucinations, feeling of detachment from reality, problems reaching an orgasm, lack of feeling or emotion, feeling overexcited, grinding of teeth
- Fainting, involuntary muscle movements, coordination and balance disorders
- Feeling dizzy (especially when rapidly standing up), decrease in 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
- Stiffness, contractions and involuntary muscular movements
- Slight changes in blood levels of liver enzymes

Rare side effects (effects that occur in 1-10 out of 10,000 users):
- Fits or seizures
- Coughing, 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)
- Decreased blood sodium levels
- Severe eye pain and reduced or blurred vision
- Abnormal, rapid or irregular heartbeat, which may lead to fainting
- Severe abdominal or back pain (may indicate a severe problem in the intestine, liver or pancreas)
- Itching, yellow skin or eyes, dark urine or flu-like symptoms – symptoms of liver inflammation (hepatitis)

Very rare side effects (effects that occur in less than 1 in 10,000 users):
- Prolonged bleeding, may be a sign of reduced number of platelets – may lead to increased risk of bruises and bleeding
- Abnormal breast milk production
- Unexpected bleeding, such as bleeding of the gums, bloody urine or vomit, or unexpected appearance of bruises or blood vessel damage (broken veins)

Side effects with unknown frequency (effects for which a frequency has not yet been determined):
- Suicidal thoughts and suicidal behavior (reported during and immediately after stopping treatment with venlafaxine, see section 2 "Special warnings regarding the use of the medicine")
- Aggression
- Dizziness (vertigo)
- Heavy vaginal bleeding shortly after birth (postpartum hemorrhage), see "Pregnancy and breastfeeding" in section 2 for further information

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

Side effects can be reported to the Ministry of Health by clicking the link " דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health website (www.health.gov.il) directing to the online form for reporting side effects or via the 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 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**:
  Viepax XR 75: Store in a dry place, below 25°C.
  Viepax XR 150, **Viepax XR 225**: Store below 25°C.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information
In addition to the active ingredient, the medicine also contains:

Viepax XR 75:
Microcrystalline cellulose, hypromellose, ethylcellulose, magnesium stearate, dibutyl sebacate, silica colloidal anhydrous, macrogol 400.
Viepax XR 150, **Viepax XR 225**:
Calcium hydrogen phosphate dihydrate, hypromellose K-100, polyacrylate dispersion 30%, polyvinyl acetate dispersion 30%, talc, magnesium stearate, macrogol-poly (vinyl alcohol) grafted copolymer, silica colloidal anhydrous, triethyl citrate, carnauba wax, purified water.

What the medicine looks like and what the package contains:
Viepax XR 75: white caplets.
Viepax XR 150, **Viepax XR 225**: white to off white mottled round shaped tablets.
Approved package sizes for **Viepax XR 75**: 7, 10, 28, 30 caplets.
Approved package sizes for **Viepax XR 150**, **Viepax XR 225**: 2, 10, 28, 30 tablets.
Not all package sizes may be marketed.

Revised in April 2024 according to MOH guidelines.

Drug registration number at the national drug registry of the Ministry of Health:
Viepax XR 75: 130-53-30839-00
Viepax XR 150: 161-41-35038-00
Viepax XR 225: 161-42-35039-00

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