

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Efexor® XR 75

Each capsule contains: Venlafaxine (as hydrochloride) 75 mg

Efexor® XR 150

Each capsule contains: Venlafaxine (as hydrochloride) 150 mg

Extended release capsules

Inactive ingredients and allergens in the preparation: See section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed for 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.

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 THIS MEDICINE INTENDED FOR?

Efexor XR is intended for treatment of patients with depression and 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: Efexor XR is an antidepressant that belongs to a group of medicines called SNRIs (serotonin and norepinephrine reuptake inhibitors). 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 effect 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 THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to venlafaxine or to any of the other ingredients in this medicine (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 Efexor 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 Efexor XR, and at least 7 days after finishing treatment with Efexor XR before starting treatment with an MAOI.

Special warnings regarding use of the medicine

Before treatment with Efexor XR, tell your doctor if:

- you are taking additional medicines that increase the risk of developing serotonin syndrome when taken together with Efexor XR (see section "Other medicines and Efexor XR").
- 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 rapid or abnormal 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 (tendency to develop bruises 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 clots), or if you are pregnant (see section "Pregnancy and breastfeeding").
- you have a history of, or if someone in your family has had, mania or bipolar disorder (manic depression).
- you have a history of aggressive behavior.
- you are pregnant, planning to become pregnant or to breastfeed (see "Pregnancy and breastfeeding" in this section).

Efexor 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 Efexor XR as it may 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.

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

Suicidal thoughts and worsening of your depression or anxiety disorder:

If you are depressed and/or suffering from an anxiety disorder, you may have thoughts of harming yourself or suicidal thoughts. These thoughts may intensify when you first start taking 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 have had suicidal thoughts or thoughts of harming yourself in the past.

- if 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 the doctor or proceed to a hospital emergency room immediately.

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, they think 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 Efexor XR. This condition may increase the risk of tooth decay. Therefore, you should be particular about oral hygiene.

Diabetes

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

Sexual dysfunction

Medicines like Efexor 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 more information.

Refer to a doctor immediately if you feel restless, that can not keep still, feel 'high' or more excited than usual, have jerky muscle movements which you cannot control. See section 4 "Side effects" for more 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. In addition, note 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. However, the doctor can prescribe this medicine to patients under the age of 18 if he thinks it is in their best interest. If your doctor has prescribed the medicine to a patient under the age of 18 and you want to consult with your doctor about it - refer back to your doctor. Inform your doctor if one or more of the symptoms listed above has appeared or worsened in patients under the age of 18 taking Efexor XR. 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

Efexor XR may sometimes cause undesirable effects that you will be unaware of, such as increased blood pressure or abnormal heartbeat, slight changes in liver enzyme levels, sodium or cholesterol levels in the blood. More infrequently, Efexor XR may impair platelet activity and cause an increase in risk of bruises or bleeding. Therefore, the doctor may occasionally perform blood tests, especially if you are taking Efexor XR for a long period of time.

Other medicines and Efexor XR

If you are taking or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or

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

- **Do not take monoamine oxidase inhibitors (MAOIs)** which are used to treat depression or Parkinson's disease, **together with Efexor XR**. Tell the doctor if you have taken medicines of this type within the last 14 days. See detailed information in subsection "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);
 - Medicines containing linezolid, an antibiotic (for treatment of infections);
 - Medicines containing moclobemide, a monoamine oxidase inhibitor (MAOI) (for treatment of depression);
 - Medicines containing sibutramine (for weight loss);
 - Medicines containing opioids (e.g., buprenorphine, tramadol, fentanyl, tapentadol, pethidine or pentazocine) to treat severe pain;
 - Medicines containing dextromethorphan (to alleviate cough);
 - Medicines containing methadone (for treatment of addiction to opiates or to treat severe pain);
 - Medicines containing 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 are not there, 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, rapid changes in blood pressure, increased reflexes, diarrhea, coma, nausea, vomiting.

The most severe form of 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, increased muscle enzymes (determined in blood tests).

Tell the doctor immediately, or proceed to the emergency room at the nearest hospital if you think you are suffering from 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 Efexor 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)
- Haloperidol or risperidone (to treat psychiatric conditions)
- Metoprolol (a beta blocker to treat hypertension and heart problems).

Using this medicine and food

Efexor XR should be taken with food (see section 3 “How to use this medicine?”).

Using this medicine and alcohol consumption

Avoid alcohol consumption while you are taking Efexor XR.

Do not drink alcohol while being treated with Efexor XR as it may 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 are planning to become pregnant, consult your doctor before taking this medicine.

Efexor 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 Efexor XR during 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 occur during the first 24 hours after the baby is born. If this happens to your baby, refer to the doctor immediately.

If you took Efexor 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 Efexor XR.

Another symptom that may appear in the newborn whose mother took Efexor 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.

Efexor XR passes into breast milk, therefore, there is a risk that the medicine will affect the baby. Hence, consult with 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.

Important information about some of this medicine's ingredients

Efexor XR 150 contains less than 1 mmol (23 mg) sodium per capsule, i.e., it is considered as sodium-free.

3. HOW TO USE THIS MEDICINE?

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

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

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

Do not exceed the recommended dose.

Efexor XR (extended-release capsules) should be taken with food, at approximately the same time each day, either in the morning or evening. Capsules must be swallowed whole with water. Do not divide, crush, chew, or dissolve the capsule in water, to avoid compromising the extended release of the medicine in the body. Alternatively, the capsule can be carefully opened and its entire contents sprinkled on a spoonful of applesauce. Swallow this mixture immediately without chewing and drink a glass of water immediately afterwards, to ensure ingestion of all of the capsule content (spheroids).

If you have liver or kidney problems, talk to your doctor, since the dosage of the medicine may be different.

Do not stop taking the medicine without consulting the doctor. Sudden discontinuation may lead to withdrawal symptoms (also see section "If you stop taking this medicine").

If you have accidentally taken a higher dosage

If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

Overdose may be life-threatening, especially with concomitant use of alcohol and/or certain medicines (see "Other medicines and Efexor XR").

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 forget to take the medicine

If you forget to take this medicine at the required 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 instead of the forgotten dose! Do not take more than the daily dose prescribed for you.

Adhere to the treatment as recommended by your doctor.

If you stop taking this 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. If the doctor thinks that you no longer need to be treated with this medicine, he will instruct you to gradually reduce the dosage before stopping treatment completely.

Sudden discontinuation of the medicine or too rapid reduction in dosage may be accompanied by side effects such as suicidal thoughts, aggressiveness, tiredness, dizziness, light-headedness, headache, insomnia, nightmares, dry mouth, decreased appetite, nausea, diarrhea, nervousness, agitation, confusion, ringing in the ears, tingling sensation or in rare instances, 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 how to gradually discontinue treatment with the medicine. This can take a period of several weeks or months. In some patients, the discontinuation may have to take place very gradually, over months or more. If you experience any of these symptoms or other worrisome symptoms, consult the doctor.

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

If you have further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Efexor XR may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Discontinue use and immediately refer to a doctor or proceed to an emergency room if one or more of the following side effects occur:

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

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

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

- 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. 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, 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 pains, tenderness or weakness. These may be signs of rhabdomyolysis.

Side effects of unknown frequency (the frequency of these effects 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 **you must tell the 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 fast or irregular heart rate, increased blood pressure.
- Eye problems, such as blurred vision, dilated pupils.
- Nerve 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 in section 3 “How to use this medicine?, If you stop taking this medicine”).
- Prolonged bleeding - if you were injured or got cut, the bleeding may persist for longer than usual.

If you notice small white balls or granules in your stools during treatment with Efexor XR, there is no need to worry. Each Efexor XR capsule contains spheroids (small white balls) that contain the active ingredient, venlafaxine. The spheroids in the capsule are released in your stomach and the active ingredient in them is slowly released during passage through the stomach and intestines. The shell of the spheroids does not dissolve and is passed out in the stool. That is to say, the required dose is absorbed despite the appearance of spheroids in the stool.

Additional side effects that may occur

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

- Dizziness, headaches, drowsiness
- Insomnia
- Nausea, dry mouth, constipation
- Sweating (including night sweats)

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

- 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 objects to nearby objects
- Ringing in the ears (tinnitus)
- Fast 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, problems with ejaculation/reaching an orgasm (in men), erectile disorders (impotence)
- Weakness, fatigue, chills
- Weight gain, weight loss
- Increased cholesterol levels

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

- 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 over-excited, grinding of teeth
- Fainting, involuntary muscle movements, coordination and balance disorders
- 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
- Lack of control of urination
- Stiffness, spasms and involuntary movements of the muscles
- Slight changes in liver enzyme levels in the blood

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

- 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 pain or severe back pain (may be indicative of 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 (may appear in up to 1 in 10,000 people):

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

- Suicidal thoughts and suicidal behavior (reported during and immediately after stopping treatment with venlafaxine, see section 2, under “Special warnings regarding use of the medicine”)
- Aggression
- Dizziness (vertigo)
- Heavy vaginal bleeding shortly after birth (postpartum hemorrhage), see “Pregnancy and breastfeeding” in section 2 for more information.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: <https://sideeffects.health.gov.il>

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept 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 a doctor.
- Do not use the medicine after the expiry date (Exp. Date) which is stated on the package. The expiry date refers to the last day of that month.
- Store in a dry place, below 25°C.

6. FURTHER INFORMATION

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

Efexor XR 75:

Microcrystalline cellulose, ethyl cellulose, hypromellose 2910, hypromellose 2208, talc.

Capsule shell: gelatin, titanium dioxide (E171), red iron oxide (E172), yellow iron oxide (E172).

Printing ink: shellac, iron oxide, propylene glycol, ammonium hydroxide, simethicone.

Efexor XR 150:

Microcrystalline cellulose, ethyl cellulose, hypromellose 2910, hypromellose 2208, talc.

Capsule shell: gelatin, red iron oxide (E172), yellow iron oxide (E172), titanium dioxide (E171).

Printing ink: shellac, propylene glycol, sodium hydroxide, povidone, titanium dioxide.

What the medicine looks like and contents of the pack:

Efexor XR 75: peach-colored, opaque capsules, marked in red with W and 75, in tray (blister) packs.

Efexor XR 150: dark orange-colored, opaque capsules, marked in white with W and 150, in tray (blister) packs.

Efexor XR 75 and Efexor XR 150 are marketed in a tray (blister) package containing 10, 14, 20, 28, 30 or 56 capsules.

Not all package types and sizes may be marketed.

Registration holder and address: Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

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

Efexor XR 75: 111.17.29394

Efexor XR 150: 111.18.29395

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