Package leaflet: Information for the patient

Venlofex 75 mg prolonged-release hard capsules
venlafaxine

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Venlofex is and what it is used for

Venlofex contains the active ingredient venlafaxine, which is an antidepressant that belongs to a group of medicines called serotonin and norepinephrine reuptake inhibitors (SNRIs). This group of medicines is used to treat depression. It is thought that people who are depressed and/or anxious have lower levels of serotonin and norepinephrine in the brain. It is not fully understood how antidepressants work, but they may help by increasing the levels of serotonin and norepinephrine in the brain.

Venlofex is a treatment for adults with depression or to prevent the recurrence of major depressive episodes. Venlofex is also a treatment for adults with the following anxiety disorders: generalised anxiety disorder, social anxiety disorder (fear or avoidance of social situations) and panic disorder (panic attacks). Treating depression or anxiety disorders properly is important to help you get better. If it is not treated, your condition may not go away and may become more serious and more difficult to treat.

2. What you need to know before you take Venlofex

Do not take Venlofex:
- if you are allergic to venlafaxine or any of the other ingredients of this medicine (listed in section 6).
- if you are also taking or have taken any time within the last 14 days any medicines known as irreversible monoamine oxidase inhibitors (MAOIs), used to treat depression or Parkinson's disease. Taking an irreversible MAOI together with venlafaxine, can cause serious or even life-threatening side effects. Also, you must wait at least 7 days after you stop taking venlafaxine before you take any MAOI (see also the sections "Serotonin syndrome" and "Other medicines and Venlofex").

Warnings and precautions

Talk to your doctor or pharmacist before taking Venlofex:

- if you use other medicines that taken together with venlafaxine could increase the risk of developing serotonin syndrome (see the section "Other medicines and Venlofex").
- if you have eye problems, such as certain kinds of glaucoma (increased pressure in the eye) or if your optician has told you that you may be at increased risk of developing glaucoma.
- if you have a history of high blood pressure or if you have recently had a heart attack.
- if you, or someone in your family, has a history of heart or heart rhythm problems.
- if you have been told you have an abnormal heart rhythm.
- if you have a history of fits (seizures).
- if you have a history of low sodium levels in your blood (hyponatraemia). Also, if you are elderly, are taking diuretics (water tablets that may cause increased production of urine) or are dehydrated (e.g. due to severe diarrhoea or being sick).
- if you have a tendency to develop bruises or a tendency to bleed easily (history of bleeding disorders), or if you are taking other medicines that thin the blood and may increase the risk of bleeding or if you are pregnant (see 'Pregnancy and breast-feeding').
- if you have a history of, or if someone in your family has had, mania or bipolar disorder (feeling over-excited or euphoric).
- If you have a history of aggressive behaviour. You may feel aggressive especially during the early stages of treatment with venlafaxine, if your dose is changed or when you stop taking.
- if you have diabetes (this medicine may affect blood sugar levels).
- if you are taking any medicine to lose weight.

<u>During treatment</u>

- This medicine may cause an increase in blood pressure or cholesterol levels. Your doctor may check your blood pressure and cholesterol levels regularly.
- If you get a sensation of restlessness or an inability to sit or stand still, which may occur during early stages of treatment, talk to your doctor or pharmacist.
- If you need to have a urine screen to check for certain medicines this medicine may affect the results. Tell your doctor or hospital staff that you are taking this medicine.
- Venlafaxine capsules contains spheroids, the insoluble portion of which is eliminated and may be seen in faeces.

<u>Thoughts of suicide and worsening of your depression or anxiety disorder</u>
If you are depressed and/or have anxiety disorders you can sometimes have thoughts of harming or killing yourself. These thoughts may be increased when you first start taking antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer. These thoughts may also occur when your dose is decreased or during discontinuation of treatment with Venlofex.

You may be more likely to think like this:
- If you have previously had thoughts about killing yourself or harming yourself
- If you are a young adult. Information from clinical trials has shown an increased risk of suicidal behaviour in young adults (less than 25 years old) with psychiatric conditions who were treated with an antidepressant.

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

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

Dry mouth
Dry mouth is reported in 10% of patients treated with venlafaxine. This may increase the risk of tooth decay (caries). Therefore, you should take special care in your dental hygiene.

Diabetes
Your blood glucose levels may be altered due to Venlofex. Therefore, the dosages of your diabetes medicines may need to be adjusted.

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

Children and adolescents
Venlofex should normally not be used for children and adolescents under 18 years. Also, you should know that patients under the age of 18 have an increased risk of side effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicines. Despite this, your doctor may prescribe this medicine for patients under 18 because he/she decides that this is in their best interests. If your doctor has prescribed this medicine for a patient under 18, and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when patients under 18 are taking Venlofex. Also, the long-term safety effects concerning growth, maturation, and cognitive and behavioural development of this medicine in this age group has not yet been demonstrated.

Other medicines and Venlofex
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription, natural and herbal remedies.

Your doctor should decide whether you can take Venlofex with other medicines.

- Do not take monoamine oxidase inhibitors (MAOIs) which are used to treat depression or Parkinson's disease with venlafaxine. Tell your doctor if you have taken these medicines within the last 14 days. (MAOIs: see the section "What you need to know before you take Venlofex").
- Serotonin syndrome:
  A potentially life-threatening condition or Neuroleptic Malignant Syndrome (NMS) -like reactions (see the section "Possible Side Effects"), may occur with venlafaxine treatment, particularly when taken with other medicines.

Examples of these medicines include:
- Triptans (used for migraine e.g. sumatriptan, zolmitriptan)
- Other medicines to treat depression, for instance SNRIs, SSRIs, tricyclics, or medicines containing lithium
- Medicines containing amphetamines (used to treat attention deficit hyperactivity disorder (ADHD), narcolepsy and obesity)
- Medicines containing linezolid, an antibiotic (used to treat infections)
- Medicines containing moclobemide, a MAOI (used to treat depression)
- Medicines containing sibutramine (used for weight loss)

- Medicines containing tramadol, fentanyl, tapentadol, pethidine or pentazocine (used to treat severe pain)
- Medicines containing dextromethorphan (used to treat coughing)
- Medicines containing methadone (used to treat opioid drug addiction or severe pain)
- Medicines containing methylene blue (used to treat high levels of methaemoglobin in the blood)
- Products containing St. John's Wort (also called *Hypericum perforatum*, a natural or herbal remedy used to treat mild depression)
- Products containing tryptophan (used for problems such as sleep and depression)
- Antipsychotics (used to treat a disease with symptoms such as hearing, seeing or sensing things which are not there, mistaken beliefs, unusual suspiciousness, unclear reasoning and becoming withdrawn).

Signs and symptoms of serotonin syndrome may include a combination of the following: restlessness, hallucinations, loss of coordination, fast heart beat, increased body temperature, fast changes in blood pressure, overactive reflexes, diarrhoea, coma, nausea, vomiting.

In its most severe form, serotonin syndrome can resemble Neuroleptic Malignant Syndrome (NMS). Signs and symptoms of NMS may include a combination of fever, fast heartbeat, sweating, severe muscle stiffness, confusion, mood changes, increased muscle enzymes (determined by a blood test).

Tell your doctor immediately, or go to the casualty department at your nearest hospital if you think serotonin syndrome or NMS is happening to you.

You must tell your doctor if you are taking medicines that can affect your heart rhythm.

Examples of these medicines include:
- Antiarrhythmics such as quinidine, amiodarone, sotalol or dofetilide (used to treat abnormal heart rhythm)
- Antipsychotics such as thioridazine (see also Serotonin syndrome above)
- Antibiotics such as erythromycin or moxifloxacin (used to treat bacterial infections)
- Antihistamines (used to treat allergy)

The following medicines may also interact with venlafaxine and should be used with caution. It is especially important to mention to your doctor or pharmacist if you are taking medicines containing:
- Medicines which inhibit certain enzymes (CYP3A4) such as
    - atazanavir, indinavir, nelfinavir, ritonavir, saquinavir (medicines used to treat HIV),
    - ketoconazole, itraconazole, voriconazole, posaconazole (antifungal medicines)
    - clarithromycin and telithromycin (antibiotics)
- Haloperidol or risperidone (to treat psychiatric conditions)
- Metoprolol (a beta blocker to treat high blood pressure and heart problems)

Venlofex with food, drink and alcohol
Venlofex should be taken with food (see Section 3 "How to take Venlofex").
You should avoid alcohol while you are taking Venlofex.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby ask your doctor or pharmacist for advice before taking this medicine. You should use venlafaxine only after discussing the potential benefits and the potential risks to your unborn child with your doctor.

Make sure your midwife and/or doctor knows you are on venlafaxine. When taken during pregnancy, similar drugs (SSRIs) may increase the risk of a serious condition in babies, called persistent pulmonary hypertension of the newborn (PPHN), making the baby breathe faster and appear bluish. These symptoms usually begin during the first 24 hours after the baby is born. If this happens to your baby you should contact your midwife and/or doctor immediately.

If you are taking this medicine during pregnancy, in addition to having trouble breathing, another symptom your baby might have when it is born is not feeding properly. If your baby has these symptoms when it is born and you are concerned, contact your doctor and/or midwife who will be able to advise you.

If you take Venlofex 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 Venlofex so they can advise you.

If you are breast-feeding ask your doctor for advice. Venlafaxine passes into breast milk. There is a risk of an effect on the baby. Therefore, you should discuss the matter with your doctor, and he/she will decide whether you should stop breast-feeding or stop the therapy with venlafaxine.

Driving and using machines
Do not drive or use any tools or machines until you know how venlafaxine affects you as this medicine may affect your judgement, thinking and ability to drive or use machines.

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to take Venlofex

Always take this medicine exactly as your doctor or pharmacist has told you. You should check with your doctor or pharmacist if you are not sure.

The usual recommended starting dose for treatment of depression, generalised anxiety disorder and social anxiety disorder is 75 mg per day. The dose can be increased by your doctor gradually, and if needed, even up to a maximum dose of 375 mg daily for depression. If you are being treated for panic disorder, your doctor will start with a lower dose (37.5 mg) and then increase the dose gradually. The maximum dose for generalised anxiety disorder, social anxiety disorder and panic disorder is 225 mg/day. Your doctor may recommend that you to take this medicine for several months depending on your condition and may check on you regularly during treatment.

Take Venlofex at approximately the same time each day, either in the morning or in the evening. Capsules must be swallowed whole with fluid and not opened, crushed, chewed or dissolved.

Venlofex should be taken with food.

If you have liver or kidney problems, talk to your doctor, since your dose of this medicine may need to be adjusted.

Do not stop taking Venlofex without talking to your doctor (see the section "If you stop taking Venlofex").

Use in children and adolescents
Venlofex is normally not recommended for use in children and adolescents (see section 2).

If you take more Venlofex than you should
Call your doctor or pharmacist immediately if you take more of this medicine than prescribed by your doctor. The symptoms of a possible overdose may include a rapid or slow heart beat or changes in the electrical activity of your heart which may be seen in tests, low blood pressure, dizziness, changes in level of alertness (ranging from sleepiness to coma), blurred vision, seizures or fits and vomiting.

If you forget to take Venlofex
If you miss a dose, take it as soon as you remember. However, if it is time for your next dose, skip the missed dose and take only a single dose as usual. Do not take a double dose to make up for a forgotten dose. Do not take more than the daily amount of Venlofex that has been prescribed for you in one day.

If you stop taking Venlofex
Do not stop taking your treatment or reduce the dose without the advice of your doctor even if you feel better. If your doctor thinks that you no longer need venlafaxine, he/she may ask you to reduce your dose slowly before stopping treatment altogether. Side effects are known to occur when people stop using this medicine, especially when Venlofex is stopped suddenly or the dose is reduced too quickly. Some patients may experience symptoms such as suicidal thoughts, aggressiveness, tiredness, dizziness, light-headedness, headache, sleeplessness, nightmares, dry mouth, loss of appetite, nausea, diarrhoea, feeling anxious, nervousness, agitation, confusion, ringing in the ears, tingling or rarely electric shock sensations, weakness, sweating, seizures, shaking, 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 venlafaxine 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 or other symptoms that are troublesome, ask your doctor for further advice.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If any of the following happen, do not take more Venlofex. **Tell your doctor immediately, or go to the casualty department at your nearest hospital:**

Uncommon (may affect up to 1 in 100 people):
- Swelling of the face, mouth, tongue, throat, hands or feet and/or a raised itch rash (hives) trouble swallowing or breathing

Rare (may affect up to 1 in 1,000 people)
- Chest tightness, wheezing, trouble swallowing or breathing
- Severe skin rash, itching or hives (elevated patches of red or pale skin that often itch)
- Severe rash which may lead to severe blisters and peeling of the skin
- Signs and symptoms of serotonin syndrome which may include restlessness, hallucinations, loss of coordination, fast heartbeat, increased body temperature, fast changes in blood pressure, overactive reflexes, diarrhoea, coma, nausea, vomiting.
  In its most severe form, serotonin syndrome can resemble Neuroleptic Malignant Syndrome (NMS). Signs and symptoms of NMS may include a combination of fever, fast heartbeat, sweating, severe muscle stiffness, confusion, increased muscle enzymes (determined by a blood test).

- Signs of infection, such as high temperature, chills, shivering, headaches, sweating, flu-like symptoms. This may be the result of a blood disorder which leads to an increased risk of infection.
- Unexplained muscle pain, tenderness or weakness. This is a sign of rhabdomyolysis.

Frequency not known (cannot be estimated from the available data)
- Signs and symptoms of a condition called "stress cardiomyopathy" which may include chest pain, shortness of breath, dizziness, fainting, irregular heartbeat.

Other side effects that you should **tell your doctor about** include

(The frequency of these side effects is included in the list "Other side effects that may occur" below):

- Coughing, wheezing and shortness of breath which may be accompanied by a high temperature
- Black (tarry) stools or blood in stools
- Itchiness, yellow skin or eyes, or dark urine, which may be symptoms of inflammation of the liver (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 disorder (muscle spasms or stiffness), seizures or fits
- Psychiatric problems, such as hyperactivity and feeling unusually overexcited
- Withdrawal effects (see the section "How to take Venlofex, if you stop taking Venlofex")
- Prolonged bleeding - if you cut or injure yourself, it may take slightly longer than usual for bleeding to stop

Do not be concerned if you see small white balls or granules in your stools after taking this medicine. Inside Venlofex capsules are spheroids (small white balls) that contain the active ingredient (venlafaxine). These spheroids are released from the capsule into your stomach. As they travel through your stomach and intestines, venlafaxine is slowly released. The spheroid "shell" does not dissolve and is passed out in your stools. So, even though you may see spheroids in your stools, your dose of medicine has been absorbed.

Other possible side effects:

Very common (may affect more than 1 in 10 people)
- Dizziness; headache
- Nausea; dry mouth
- Sleepiness
- Excessive sweating (including night sweats)
- Difficulty sleeping (insomnia)
- Constipation

Common (may affect up to 1 in 10 people)
- Appetite decreased
- Confusion; feeling separated (or detached) from yourself; lack of orgasm; decreased libido; agitation; nervousness; abnormal dreams; agitation
- Visual disturbance including blurred vision; dilated pupils; inability of the eye to automatically change focus from distant to near objects
- Ringing in the ears (tinnitus)
- Increase in blood pressure; flushing

- Yawning
- Being sick (vomiting); diarrhoea
- Increased frequency in urination; inability to pass urine; difficulties passing urine
- Menstrual irregularities such as increased bleeding or increased irregular bleeding; abnormal ejaculation/orgasm (males); erectile dysfunction (impotence)
- Weakness (asthenia); fatigue; chills
- Increased cholesterol in the blood
- Shortness of breath
- Mild rash, itching
- Weight gain; weight loss
- A sensation of restlessness or an inability to sit or stand still; pins and needles; altered taste sensation; increased muscle tonus
- Fast heartbeat, palpitations

Uncommon (may affect up to 1 in 100 people)
- Over activity, racing thoughts and decreased need for sleep (mania)
- Hallucinations; feeling separated (or detached) from reality; abnormal orgasm; lack of feeling or emotion; feeling over-excited; grinding of the teeth
- Fainting; involuntary movements of the muscles; uncontrollable twitching, jerking or writhing movements, impaired coordination and balance
- Feeling dizzy (particularly when standing up too quickly); decrease in low blood pressure
- Vomiting blood, black tarry stool (faeces) or blood in stools, which can be a sign of internal bleeding
- Sensitivity to sunlight; bruising (ecchymosis); abnormal hair loss, hives (urticaria)
- Low blood pressure
- Slight changes in blood levels of liver enzymes which may be seen in blood test
- Inability to control urination
- Stiffness, spasms and involuntary movements of the muscles

Rare (may affect up to 1 in 1,000 people)
- Decrease in blood sodium levels which may be seen in blood tests
- Disorientation and confusion often accompanied by hallucination (delirium)
- Coughing, wheezing and shortness of breath which may be accompanied by a high temperature
- Excessive water intake (known as SIADH)
- Severe eye pain and decreased or blurred vision
- Abnormal, rapid or irregular heartbeat, which could lead to fainting
- Severe abdominal or back pains (which could indicate a serious problem in the gut, liver or pancreas)
- Itchiness, yellow skin or eyes, dark urine, or flu-like symptoms, which are symptoms of inflammation of the liver (hepatitis)

Very rare (may affect up to 1 in 10,000 people)
- Abnormal breast milk production
- Prolonged bleeding, which may be a sign of reduced number of platelets in your blood, leading to an increased risk of bruising or bleeding
- Unexpected bleeding, e.g. bleeding gums, blood in the urine or in vomit, or the appearance of unexpected bruises or broken blood vessels (broken veins)

Not known (frequency cannot be estimated from the available data)
- Suicidal ideation and suicidal behaviours; cases of suicidal ideation and suicidal behaviours have been reported during venlafaxine therapy or early after treatment discontinuation (see section 2, What you need to know before you take Venlofex)
- Aggression
- Vertigo
- Heavy vaginal bleeding shortly after birth (postpartum haemorrhage), see Pregnancy and breast-feeding, in section 2 for more information.

Venlofex sometimes causes unwanted effects that you may not be aware of, such as increases in blood pressure or abnormal heart beat; slight changes in blood levels of liver enzymes, sodium or cholesterol. More rarely, Venlofex may reduce the function of platelets in your blood, leading to an increased risk of bruising or bleeding. Therefore, your doctor may wish to do blood tests occasionally, particularly if you have been taking Venlofex for a long time

Additional side effects in children and adolescents
Although this medicine is not normally recommended in children and adolescents, hostility, self-harm, stomach aches, indigestion and heartburn and muscle pain have additionally been reported.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance. Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Venlofex

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date, which is stated on the label/carton after EXP. The expiry date refers to the last day of that month.
This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Venlofex contains
The active substance is venlafaxine.
Each prolonged-release capsule hard contains venlafaxine hydrochloride equivalent to 75 mg of venlafaxine (as the hydrochloride). The other ingredients are: hypromellose, ammonio methacrylate copolymer, sodium laurilsulfate, magnesium stearate, basic butylated methacrylate copolymer.
The capsule shell contains: titanium dioxide E171, gelatin, red iron oxide E172.
Printing Ink: shellac glaze, iron oxide black.

What Venlofex looks like and contents of the pack
Opaque, flesh hard capsules, marked with ‘VEN’ on cap of the capsule and ‘75’ on the body.

Venlofex prolonged-release hard capsules are available in blister packs of 7, 10, 14, 20, 25, 28, 30, 30x1, 50, 56, 70, 90, 100, 500, 1000 and in multipacks of 90 comprising 3 cartons, each containing 30 or 100 comprising 2 cartons, each containing 50 capsules and bottles containing 7, 10, 14, 20, 25, 28, 30, 50, 56, 70, 90, 100 and 250 capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
McDermott Laboratories Ltd. T/A Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland.

Manufacturers
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This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Venlafaxin Arcana retard - Kapseln
Belgium and The Netherlands	Venlafaxine Retard Mylan
Sweden, Czech Republic and Slovakia	Venlafaxin Mylan
France	VENLAFAXINE Mylan gélule à libération prolongée
Germany	Venlafaxin dura Hartkapseln, retardiert
Greece	Venlafaxine/Mylan 75mg/CAP Καψάκιο παρατεταμένης αποδέσμευσης, σκληρό
Ireland	Venlofex
Italy	Venlafaxina Mylan Generics
Poland	Faxigen XL
Portugal	VENLAFAXINA Mylan
Spain	Venlamylan Retard cápsulas duras de liberación prolongada EFG
United Kingdom	Vexarin XL prolonged release capsules, hard

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