

Package leaflet: Information for the patient

Vexarin XL 75 mg Prolonged-release capsules, hard Vexarin XL 150 mg Prolonged-release capsules, hard

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 Vexarin XL is and what it is used for
2. What you need to know before you take Vexarin XL
3. How to take Vexarin XL
4. Possible side effects
5. How to store Vexarin XL
6. Contents of the pack and other information

1. What Vexarin XL is and what it is used for

Vexarin XL contains the active substance venlafaxine.

Vexarin XL 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 and other conditions such as anxiety disorders. It is thought that people who are depressed and/or anxious have lower levels of serotonin and noradrenaline in the brain. It is not fully understood how antidepressants work, but they may help by increasing the levels of serotonin and noradrenaline in the brain.

Vexarin XL is a treatment for adults with depression. Vexarin XL 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 Vexarin XL

Do not take Vexarin XL

- 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 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 Vexarin XL, can cause serious or even life-threatening side effects. Also, you must wait at least 7 days after you stop taking Vexarin XL before you take any MAOI (see also the section "Other medicines and Vexarin XL" and the information in that section about "Serotonin Syndrome").

Warnings and precautions

Talk to your doctor or pharmacist before taking Vexarin XL:

- If you use other medicines that taken together with Vexarin XL could increase the risk of developing serotonin syndrome (see the section “Other medicines and Vexarin XL”)
- If you have eye problems, such as certain kinds of glaucoma (increased pressure in the eye)
- If you have a history of high blood pressure
- If you have a history of heart 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)
- 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 may increase the risk of bleeding e.g. warfarin (used to prevent blood clots)
- 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.

Vexarin XL may cause a sensation of restlessness or an inability to sit or stand still during the first few weeks of treatment. You should tell your doctor if this happens to you.

If any of these conditions apply to you, please talk with your doctor before taking Vexarin XL.

Thoughts of suicide and worsening of your depression or anxiety disorder

If you are depressed and/or have anxiety disorders you can sometimes have thoughts of harming or killing yourself. These may be increased when you first start taking antidepressants, since these medicines all take time to work, usually about two weeks, but sometimes longer.

You may be more likely to think like this:

- If you have previously had thoughts about killing 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 Vexarin XL. Therefore, the dosage of your diabetes medicines may need to be adjusted.

Effect on urine drug screens

If you are having a urine drug screen, taking Vexarin XL may cause positive results for phencyclidine (PCP) or amphetamine when some test methods are used, even though you may not be taking PCP or amphetamine. If this happens, a more specific test can be performed.

Children and adolescents

Vexarin XL should normally not be used in children and adolescents under the age of 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 Vexarin XL for patients under 18 because he/she decides that this is in their best interests. If your doctor has prescribed Vexarin XL 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 Vexarin XL. Also, the long-term safety effects concerning growth, maturation, and cognitive and behavioural development of Vexarin XL in this age group have not yet been demonstrated.

Other medicines and Vexarin XL

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

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

Do not start or stop taking any medicines, including those bought without a prescription, natural and herbal remedies, before checking with your doctor or pharmacist.

- Monoamine oxidase inhibitors which are used to treat depression or Parkinson's disease **must not be taken with Vexarin XL**. 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 Vexarin XL").
- **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)
- Other medicines to treat depression, for instance SNRIs, SSRIs, tricyclics, or medicines containing lithium
- 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)
- Opioid medicines (used to treat moderate to severe pain such as tramadol, fentanyl, tapentadol, pethidine, methadone, pentazocine)
- 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)
- Dextromethorphan (used to treat coughs)
- Medicines containing methylene blue (used to treat high levels of methaemoglobin in the blood or certain types of blood poisoning)
- 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 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).

Tell your doctor immediately, or go to the casualty department at your nearest hospital if you think serotonin syndrome 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, dofetilide (used to treat abnormal heart rhythms)
- antipsychotics such as thioridazine
- antibiotics such as erythromycin or moxifloxacin
- antihistamines (used to treat allergies).

The following medicines may also interact with Vexarin XL and should be used with caution. It is especially important to mention to your 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 high blood pressure and heart problems)

Vexarin XL with alcohol

You should avoid alcohol while you are taking Vexarin XL.

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.

Tell your doctor if you become pregnant, or you are trying to become pregnant. You should take 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 Vexarin XL. 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, other symptoms your baby might have when it is born is not feeding properly, in addition to having trouble breathing. 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.

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 Vexarin XL.

Driving and using machines

Do not drive or use any tools or machines until you know how Vexarin XL affects you.

3. How to take Vexarin XL

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

The recommended starting dose for the treatment of depression, generalised anxiety disorder and social anxiety disorder is 75 mg per day. The dose can be raised 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 to 75 mg per day. The maximum dose for generalised anxiety disorder, social anxiety disorder and panic disorder is 225 mg/day.

Take Vexarin XL 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.

Vexarin XL should be taken with food.

If you have liver or kidney problems, talk to your doctor, since your dose of Vexarin XL may need to be different.

Do not stop taking Vexarin XL without talking to your doctor (see the section “If you stop taking Vexarin XL”).

If you take more Vexarin XL than you should

Call your doctor or pharmacist immediately if you take more than the amount of Vexarin XL prescribed by your doctor. The symptoms of a possible overdose may include a rapid heartbeat, changes in level of alertness (ranging from sleepiness to coma), blurred vision, seizures or fits, and vomiting.

If you forget to take Vexarin XL

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 Vexarin XL that has been prescribed for you in one day.

If you stop taking Vexarin XL

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 Vexarin XL, he/she may ask you to reduce your dose slowly before stopping treatment altogether. Side effects are known to occur when people stop using Vexarin XL, especially when Vexarin XL is stopped suddenly or the dose is reduced too quickly. Some patients may experience symptoms such as tiredness, dizziness, light-headedness, headache, sleeplessness, nightmares, dry mouth, loss of appetite, nausea, diarrhoea, nervousness, agitation, confusion, ringing in the ears, tingling or rarely electric shock sensations, weakness, sweating, seizures, or flu-like symptoms.

Your doctor will advise you on how you should gradually discontinue Vexarin XL treatment. 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 Vexarin XL. 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, tongue, throat, hands, or feet.

Rare (may affect up to 1 in 1,000 people):

- 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).

- Severe skin reaction with the peeling of the top layer of the skin, severe blisters and bleeding in the skin and also in the lips, eyes, mouth, nose and genitals.
- Chest tightness, wheezing, trouble swallowing or breathing
- Signs of frequent infection such as high temperature, sore throat, flu-like symptoms or ulcers in your mouth or throat, tiredness, shortness of breath, looking pale or bruising or bleeding more easily than normal. These may be due to reduction in certain type of blood cells
- Severe rash, itching, or hives (elevated patches of red or pale skin that often itch)
- Unexplained muscle pain, tenderness or weakness (rhabdomyolysis)

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

Common (may affect up to 1 in 10 people):

- Heart problems, such as fast or irregular heart rate, increased blood pressure
- Nerve problems, such as pins and needles
- Inability to pass urine

Uncommon (may affect up to 1 in 100 people)

- Vomiting blood, black (tarry) stools or blood in stools, which can be a sign of internal bleeding
- Psychiatric problems, such as hyperactivity and feeling unusually overexcited

Rare (may affect up to 1 in 1,000 people)

- Seizures or fits
- Pain in the upper abdomen and back, feeling or being sick which may be caused by inflammation of pancreas (pancreatitis)
- Yellow skin or eyes, itchiness or dark urine, which may be symptoms of inflammation of the liver (hepatitis)
- Eye problems, such as blurred vision, dilated pupils
- Coughing, wheezing, shortness of breath and a high temperature

Very rare (may affect up to 1 in 10,000 people)

- Prolonged bleeding – if you cut or injure yourself, it may take slightly longer than usual for bleeding to stop.
- Nerve problems such as movement disorders

Not known (cannot be estimated from the available data)

- Withdrawal effects (see the section “How to take Vexarin XL, if you stop taking Vexarin XL”)
- 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 Vexarin XL)

Do not be concerned if you see small white balls or granules in your stools after taking this medicine. Inside Vexarin XL 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 include:

Very common (may affect more than 1 in 10 people)

- Dizziness; headache
- Nausea; dry mouth
- Insomnia
- Sweating (including night sweats)
- Drowsiness
- Constipation

Common (may affect up to 1 in 10 people)

- Appetite decreased
- Confusion; feeling separated (or detached) from yourself; lack of orgasm; decreased libido; nervousness; abnormal dreams
- Tremor; a sensation of restlessness or an inability to sit or stand still, increased muscle tightness
- 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)
- Palpitations
- Increase in blood pressure; flushing
- Rash, itching
- Yawning
- Agitation
- Vomiting; diarrhoea
- Increased frequency in urination; 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
- Altered taste sensation
- Fast heartbeat
- Shortness of breath
- Weight gain, weight loss

Uncommon (may affect up to 1 in 100 people)

- Hallucinations; feeling separated (or detached) from reality; abnormal orgasm (females); lack of feeling or emotion; feeling underexcited; grinding of the teeth
- Fainting; involuntary movement of the muscles; impaired coordination and balance
- Feeling dizzy (particularly when standing up too quickly)
- Sensitivity to sunlight; bruising; hives; abnormal hair loss
- Inability to control urination
- Over activity, racing thoughts and decreased need for sleep (mania)
- Decrease in blood pressure
- Changes in blood levels of liver enzymes
- Stiffness, spasms and involuntary movements of the muscles

Rare (may affect up to 1 in 1,000 people)

- Excessive water intake (known as SIADH)
- Decrease in blood sodium levels
- Disorientation and confusion often accompanied by hallucination (delirium)
- Uncontrolled muscle spasms affecting the eyes, head, neck and the body
- Severe eye pain, hazy or blurred vision with rainbow coloured circles around bright lights
- Abnormal, rapid or irregular heartbeat, which could lead to fainting

Very rare (may affect up to 1 in 10,000 people)

- An increase in blood levels of a hormone called prolactin which may lead to abnormal breast milk production
- Unexpected bleeding, e.g. bleeding gums, blood in the urine or the appearance of unexpected bruises or broken blood vessels (broken veins)

Not known (frequency cannot be estimated from the available data)

- Aggression
- Vertigo

Additional side effects seen in children and adolescents

In clinical trials, the following side effects were also seen in children and adolescents:

- Unfriendliness (hostility)
- Stomach pain
- Indigestion
- Nosebleeds
- Muscle pain

Venlafaxine 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 or liver enzymes, sodium or cholesterol. More rarely, venlafaxine 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 venlafaxine for a long time.

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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971 FREE Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Vexarin XL

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 packaging after EXP. The expiry date refers to the last day of that month.

This medicine does not require 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 Vexarin XL contains**

The active substance is venlafaxine.

Each prolonged-release capsule, hard contains venlafaxine hydrochloride, equivalent to 75 mg or 150 mg of venlafaxine (as the hydrochloride). The other ingredients are:

Capsule content:

Microcrystalline cellulose, hydroxypropyl cellulose, talc

Sub-coating: Hypromellose, macrogol

Prolonged-release coating: Ethyl cellulose, hypromellose

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

Printing Ink: Shellac, propylene glycol, iron oxide black (E172), potassium hydroxide

What Vexarin XL looks like and contents of the pack

75 mg - Size 1, hard, gelatin capsule with opaque flesh (pink) cap and body, axially printed with "MYLAN" over "VE75" in black ink.

150 mg - Size 0, hard, gelatin capsule with opaque dark orange cap and body, axially printed with "MYLAN" over "VE150" in black ink.

Aclar/PVC-Al, OPA/Al/PVC-Al and PVC/PVDC blister packs of 7, 10, 14, 28, 30, 50, 56, 60, 84, 90, 98, 100 capsules and HDPE bottles containing 30 and 250 capsules. Not all pack sizes may be marketed.

Marketing Authorisation Holder

McDermott Laboratories Limited t/a Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13

Manufacturer

McDermott Laboratories Limited t/a Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13

Generics [UK] Ltd., Station Close, Potter Bar, Hertfordshire, EN6 1TL, UK

Mylan Hungary Kft., H-2900, Komárom, Mylan utca 1, Hungary

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

Austria	Venlafaxin Mylan 75 mg, 150 mg Retardkapseln
Belgium	Venlamylan 37,5 mg, 75 mg, 150 mg capsules met verlengde afgifte, hard
Czech Republic	Venlamyl 75 mg, 150 mg, tvrdé tobolky s prodlouženým uvolňováním
Denmark	Vefamyl Mylan
France	Venlafaxine MYLAN PHARMA LP 37,5 mg, 75 mg, gélule à libération prolongée
Ireland	Vexarin XL 37.5 mg, 75 mg, 150 mg Prolonged-release capsules, hard
Netherlands	Venlafaxine Mylan 37,5 mg, 75 mg, 150 mg, capsules met verlengde afgifte, hard
Portugal	Venlafaxina Anova
Slovenia	Nefexyl 75 mg, 150 mg trde kapsule s podaljšaním sproščanjem
Spain	Venlafaxina Retard Mylan Pharmaceuticals 75/150 mg cápsulas duras de liberación prolongada EFG
Sweden	Vefamyl
United Kingdom	Amphero XL 75 mg and 150 mg Prolonged Release Capsules

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