

PACKAGE LEAFLET: INFORMATION FOR THE USER

Venlalic® XL 225mg prolonged-release tablets (venlafaxine hydrochloride)

Your medicine is available using the name Venlalic XL 225mg prolonged-release tablets but will be referred to as Venlalic XL throughout this leaflet. Other strengths 37.5mg, 75mg, and 150mg are also available.

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 please 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:

- What Venlalic XL is and what it is used for
- What you need to know before you take Venlalic XL
- How to take Venlalic XL
- Possible side effects
- How to store Venlalic XL
- Contents of the pack and other information

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

Venlalic 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.

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

Do not take Venlalic 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 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 Venlalic XL, can cause serious or even life-threatening side effects. Also, you must wait at least 7 days after you stop taking Venlalic XL before you take any MAOI (see also the sections entitled "Other medicines and Venlalic XL" and the information in that section about "Serotonin syndrome").

Warnings and precautions

Talk to your doctor before taking Venlalic XL

- If you use other medicines that taken concomitantly with Venlalic XL could increase the risk of developing serotonin syndrome (see the section "Other medicines and Venlalic XL").
- If you have a swallowing, stomach or intestinal disorder that reduces your ability to swallow or pass foods by normal bowel movements.
- 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 that 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 your cholesterol levels get higher.
- 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.

Venlalic 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 Venlalic 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 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 Venlalic XL. Therefore, the dosages of your diabetes medicines may need to be adjusted.

Use in children and adolescents under the age of 18 years

Venlalic XL should normally not be used for children and adolescents under 18 years. Also, you should know that patients under 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 Venlalic 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 Venlalic XL. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of Venlalic XL in this age group has not yet been demonstrated.

Other medicines and Venlalic 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 Venlalic 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 Venlalic 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 Venlalic XL").
- Serotonin syndrome: 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)
- Medicines to treat depression, for instance SNRI, SSRIs, tricyclics, or medicines containing lithium
- Medicines containing linezolid, an antibiotic (used to treat infections)
- Medicines containing moclobemide, a reversible 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 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.

Cases of unintended pregnancies have been reported in patients taking oral contraceptives while on venlafaxine. It is not yet known if these pregnancies were a result of the combination with venlafaxine. Tell your doctor if you are taking oral contraceptives.

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 Venlalic 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, itraconazole, voriconazole, posaconazole (antifungal medicines)
- Clarithromycin, telithromycin (antibiotics used to treat infections)
- Atazanavir, indinavir, nelfinavir, ritonavir, saquinavir (used to treat HIV infection)
- Haloperidol or risperidone (to treat psychiatric conditions)
- Metoprolol (a beta blocker to treat high blood pressure and heart problems)

Venlalic XL with food, drink and alcohol

Venlalic XL should be taken with food (see section 3 "How to take Venlalic XL").

You should avoid alcohol while you are taking Venlalic XL.

Pregnancy, breast-feeding and fertility

Tell your doctor if you become pregnant, or you are trying to become pregnant. You should use Venlalic XL 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 Venlalic 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.

Venlalic XL passes into breast milk. There is a risk of an effect on the baby, which may cause symptoms such as crying, irritability and abnormal sleep patterns. Symptoms consistent with venlafaxine drug discontinuation can also occur after stopping breast-feeding. 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 Venlalic XL.

Driving and using machines

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

Important information about some of the ingredients of Venlalic XL

This medicine contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Venlalic XL

Always take this medicine exactly as your doctor has told you. 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 75mg per day. The dose can be raised by your doctor gradually, and if needed, even up to a maximum dose of 375mg daily for depression. If you are being treated for panic disorder, your doctor will start with a lower dose (37.5mg) and then increase the dose gradually. The maximum dose for generalised anxiety disorder, social anxiety disorder and panic disorder is 225mg/day.

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

Venlalic XL should be taken with food.

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

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

If you take more Venlalic XL than you should

Call your doctor or pharmacist immediately if you take more than the amount of Venlalic 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 Venlalic 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 more than the daily amount of Venlalic XL that has been prescribed for you in one day.

If you stop taking Venlalic 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 Venlalic 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 Venlalic XL, especially when Venlalic XL is stopped suddenly or the dose is reduced too quickly. Some patients may experience symptoms such as tiredness, dizziness, light-headedness, headache, sleeplessness, sensation that everything around you is spinning or moving (vertigo), 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 Venlalic 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, Venlalic XL can cause side effects, although not everybody gets them.

Do not be concerned if you see a tablet in your stools after taking Venlalic XL. As the tablet travels the length of your gastro-intestinal tract, venlafaxine is slowly released. The shape of the tablet remains undissolved and is eliminated in your stools. Therefore, even though you may see a tablet in your stools, your dose of venlafaxine has been absorbed.

Allergic reactions

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

- Chest tightness, wheezing, trouble swallowing or breathing
- Swelling of the face, throat, hands or feet
- Feeling nervous or anxious, dizziness, throbbing sensations, sudden reddening of the skin and/or a warm feeling
- Severe rash, itching or hives (elevated patches of red or pale skin that often itch)
- 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).

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

- Coughing, wheezing, shortness of breath and a high temperature
- Black (tarry) stools or blood in stools
- Yellow skin or eyes, itchiness 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, seizures or fits
- Psychiatric problems, such as hyperactivity and euphoria (feeling unusually overexcited)
- Withdrawal effects (see the section "How to take Venlalic XL", "If you stop taking Venlalic XL")
- Prolonged bleeding – if you cut or injure yourself, it may take slightly longer than usual for bleeding to stop.

Complete side effect listing

Very common

(may affect more than 1 in 10 people)

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

Common (may affect up to 1 in 10 people)

- Appetite decreased
- Confusion; feeling separated (or detached) from yourself; lack of orgasm; decreased libido; nervousness; insomnia; abnormal dreams
- Drowsiness; tremor; pins and needles; increased muscle tone
- 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
- Yawning
- Vomiting; constipation; 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

Uncommon (may affect up to 1 in 100 people)

- Hallucinations; feeling separated (or detached) from reality; agitation; abnormal orgasm (females); lack of feeling or emotion; feeling over-excited; grinding of the teeth
- A sensation of restlessness or an inability to sit or stand still; fainting; involuntary movements of the muscles; impaired coordination and balance; altered taste sensation
- Fast heartbeat; feeling dizzy (particularly when standing up too quickly)
- Shortness of breath
- Vomiting blood, black tarry stools (faeces) or blood in stools, which can be a sign of internal bleeding
- General swelling of the skin especially the face, mouth, tongue, throat area or hands and feet and/or a raised itchy rash (hives) may be present; sensitivity to sunlight; bruising; rash; abnormal hair loss
- Inability to pass urine
- Weight gain; weight loss

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

- Seizures or fits
- Inability to control urination
- Over activity, racing thoughts and decreased need for sleep (mania)

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

- Reduced number of platelets in your blood, leading to an increased risk of bruising or bleeding; blood disorders which may lead to an increased risk of infection
- Swollen face or tongue, shortness of breath or difficulty breathing, often with skin rashes (this may be a serious allergic reaction)
- Excessive water intake (known as SIADH)
- Decrease in blood sodium levels
- 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 Venlalic XL")
- Disorientation and confusion often accompanied by hallucination (delirium); aggression
- A high temperature with rigid muscles, confusion or agitation, and sweating, or if you experience jerky muscle movements which you can't control, these may be symptoms of serious conditions known as neuroleptic malignant syndrome; euphoric feelings, drowsiness, sustained rapid eye movement, clumsiness, restlessness, feeling of being drunk, sweating or rigid muscles, which are symptoms of serotonin syndrome; stiffness, spasms and involuntary movements of the muscles
- Severe eye pain and decreased or blurred vision
- Vertigo
- Decrease in blood pressure; abnormal, rapid or irregular heartbeat, which could lead to fainting; 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)
- Coughing, wheezing, shortness of breath and a high temperature, which are symptoms of inflammation of the lungs associated with an increase in white blood cells (pulmonary eosinophilia)
- 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); slight changes in blood levels of liver enzymes
- Skin rash, which may lead to severe blistering and peeling of the skin; itching; mild rash
- Unexplained muscle pain, tenderness or weakness (rhabdomyolysis)
- Abnormal breast milk production

Venlalic XL sometimes causes unwanted effects that you may not be aware of, such as increases in blood pressure or abnormal heartbeat; slight changes in blood levels or liver enzymes, sodium or cholesterol. More rarely, Venlalic XL 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 Venlalic XL for a long time.

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Venlalic XL

- **KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.**
- Do not use Venlalic XL after the expiry date (Exp) which is stated on the carton and blister labels. The expiry date refers to the last day of that month.
- Do not store above 30°C.
- Store in the original package in order to protect from moisture.
- If your doctor decides to stop the treatment, return any leftover medicine to the pharmacist. Only keep it if your doctor tells you to.
- If your medicine appears to be discoloured or show any other signs of deterioration, please return to your pharmacist who will advise you further.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Venlalic XL contains

The active substance is venlafaxine. Each prolonged-release tablet contains 225mg venlafaxine (as hydrochloride).

The other ingredients are **Core:** mannitol (E421), povidone K-90, macrogol 400, microcrystalline cellulose, colloidal anhydrous silica and magnesium stearate. **Coat:** cellulose acetate, macrogol 400 and Opadry Y 30 18037 (a mixture of hypromellose, lactose monohydrate, titanium dioxide (E171) and triacetin).

What Venlalic XL looks like and contents of the pack

Venlalic XL are round, biconvex, plain white tablets with a laser hole on one side.

Venlalic XL is available in blister packs of 28 tablets.

Manufacturer

Manufactured by:
Laboratorios LICONSA S.A., Avda. Miralcampo No 7, Poligono Industrial Miralcampo, 19200 Azuqueca de Henares (Guadalajara), Spain
or
Italfarmaco S.p.A., Viale F. Testi, 330, 20126 Milan, Italy.

Procured from within the EU and repackaged by:
Doncaster Pharmaceuticals Group Ltd., Kirk Sandall, Doncaster, DN3 1QR.

Product Licence holder:
Landmark Pharma Ltd., 7 Regents Drive, Prudhoe, Northumberland, NE42 6PX.

PL No: 21828/0608

POM

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**Blind or partially sighted?
Is this leaflet hard to see or read?
Call +44 (0) 1302 365000
(Regulatory)**

**Please be ready to give the following information:
Product name:
Venlalic XL 225mg
prolonged-release tablets
Reference No: 21828/0608**

PACKAGE LEAFLET: INFORMATION FOR THE USER

Axyven XL 225mg prolonged-release tablets (venlafaxine hydrochloride)

Your medicine is available using the name Axyven XL 225mg prolonged-release tablets but will be referred to as Axyven XL throughout this leaflet. Other strengths 37.5mg, 75mg, and 150mg are also available.

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 please 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:

- What Axyven XL is and what it is used for
- What you need to know before you take Axyven XL
- How to take Axyven XL
- Possible side effects
- How to store Axyven XL
- Contents of the pack and other information

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

Axyven 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.

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

Do not take Axyven 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 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 Axyven XL, can cause serious or even life-threatening side effects. Also, you must wait at least 7 days after you stop taking Axyven XL before you take any MAOI (see also the sections entitled "Other medicines and Axyven XL" and the information in that section about "Serotonin syndrome").

Warnings and precautions

Talk to your doctor before taking Axyven XL

- If you use other medicines that taken concomitantly with Axyven XL could increase the risk of developing serotonin syndrome (see the section "Other medicines and Axyven XL").
- If you have a swallowing, stomach or intestinal disorder that reduces your ability to swallow or pass foods by normal bowel movements.
- 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 that 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 your cholesterol levels get higher.
- 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.

Axyven 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 Axyven 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 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 Axyven XL. Therefore, the dosages of your diabetes medicines may need to be adjusted.

Use in children and adolescents under the age of 18 years

Axyven XL should normally not be used for children and adolescents under 18 years. Also, you should know that patients under 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 Axyven 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 Axyven XL. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of Axyven XL in this age group has not yet been demonstrated.

Other medicines and Axyven XL

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

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 - Medicines containing moclobemide, a reversible 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 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.

Cases of unintended pregnancies have been reported in patients taking oral contraceptives while on venlafaxine. It is not yet known if these pregnancies were a result of the combination with venlafaxine. Tell your doctor if you are taking oral contraceptives.

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 Axyven 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, itraconazole, voriconazole, posaconazole (antifungal medicines)
- Clarithromycin, telithromycin (antibiotics used to treat infections)
- Atazanavir, indinavir, nelfinavir, ritonavir, saquinavir (used to treat HIV infection)
- Haloperidol or risperidone (to treat psychiatric conditions)
- Metoprolol (a beta blocker to treat high blood pressure and heart problems)

Axyven XL with food, drink and alcohol

Axyven XL should be taken with food (see section 3 "How to take Axyven XL").

You should avoid alcohol while you are taking Axyven XL.

Pregnancy, breast-feeding and fertility

Tell your doctor if you become pregnant, or you are trying to become pregnant. You should use Axyven XL 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 Axyven 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.

Axyven XL passes into breast milk. There is a risk of an effect on the baby, which may cause symptoms such as crying, irritability and abnormal sleep patterns. Symptoms consistent with venlafaxine drug discontinuation can also occur after stopping breast-feeding. 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 Axyven XL.

Driving and using machines

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

Important information about some of the ingredients of Axyven XL

This medicine contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Axyven XL

Always take this medicine exactly as your doctor has told you. 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 75mg per day. The dose can be raised by your doctor gradually, and if needed, even up to a maximum dose of 375mg daily for depression. If you are being treated for panic disorder, your doctor will start with a lower dose (37.5mg) and then increase the dose gradually. The maximum dose for generalised anxiety disorder, social anxiety disorder and panic disorder is 225mg/day.

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

Axyven XL should be taken with food.

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

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

If you take more Axyven XL than you should

Call your doctor or pharmacist immediately if you take more than the amount of Axyven 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 Axyven 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 more than the daily amount of Axyven XL that has been prescribed for you in one day.

If you stop taking Axyven 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 Axyven 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 Axyven XL, especially when Axyven XL is stopped suddenly or the dose is reduced too quickly. Some patients may experience symptoms such as tiredness, dizziness, light-headedness, headache, sleeplessness, sensation that everything around you is spinning or moving (vertigo), 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 Axyven 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, Axyven XL can cause side effects, although not everybody gets them.

Do not be concerned if you see a tablet in your stools after taking Axyven XL. As the tablet travels the length of your gastro-intestinal tract, venlafaxine is slowly released. The shape of the tablet remains undissolved and is eliminated in your stools. Therefore, even though you may see a tablet in your stools, your dose of venlafaxine has been absorbed.

Allergic reactions

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

- Chest tightness, wheezing, trouble swallowing or breathing
- Swelling of the face, throat, hands or feet
- Feeling nervous or anxious, dizziness, throbbing sensations, sudden reddening of the skin and/or a warm feeling
- Severe rash, itching or hives (elevated patches of red or pale skin that often itch)
- 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).

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

- Coughing, wheezing, shortness of breath and a high temperature
- Black (tarry) stools or blood in stools
- Yellow skin or eyes, itchiness 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, seizures or fits
- Psychiatric problems, such as hyperactivity and euphoria (feeling unusually overexcited)
- Withdrawal effects (see the section "How to take Axyven XL", "If you stop taking Axyven XL")
- Prolonged bleeding – if you cut or injure yourself, it may take slightly longer than usual for bleeding to stop.

Complete side effect listing

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

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

Common (may affect up to 1 in 10 people)

- Appetite decreased
- Confusion; feeling separated (or detached) from yourself; lack of orgasm; decreased libido; nervousness; insomnia; abnormal dreams
- Drowsiness; tremor; pins and needles; increased muscle tone
- 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
- Yawning
- Vomiting; constipation; 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

Uncommon (may affect up to 1 in 100 people)

- Hallucinations; feeling separated (or detached) from reality; agitation; abnormal orgasm (females); lack of feeling or emotion; feeling over-excited; grinding of the teeth
- A sensation of restlessness or an inability to sit or stand still; fainting; involuntary movements of the muscles; impaired coordination and balance; altered taste sensation
- Fast heartbeat; feeling dizzy (particularly when standing up too quickly)
- Shortness of breath
- Vomiting blood, black tarry stools (faeces) or blood in stools, which can be a sign of internal bleeding
- General swelling of the skin especially the face, mouth, tongue, throat area or hands and feet and/or a raised itchy rash (hives) may be present; sensitivity to sunlight; bruising; rash; abnormal hair loss
- Inability to pass urine
- Weight gain; weight loss

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

- Seizures or fits
- Inability to control urination
- Over activity, racing thoughts and decreased need for sleep (mania)

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

- Reduced number of platelets in your blood, leading to an increased risk of bruising or bleeding; blood disorders which may lead to an increased risk of infection
- Swollen face or tongue, shortness of breath or difficulty breathing, often with skin rashes (this may be a serious allergic reaction)
- Excessive water intake (known as SIADH)
- Decrease in blood sodium levels
- 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 Axyven XL")
- Disorientation and confusion often accompanied by hallucination (delirium); aggression
- A high temperature with rigid muscles, confusion or agitation, and sweating, or if you experience jerky muscle movements which you can't control, these may be symptoms of serious conditions known as neuroleptic malignant syndrome; euphoric feelings, drowsiness, sustained rapid eye movement, clumsiness, restlessness, feeling of being drunk, sweating or rigid muscles, which are symptoms of serotonin syndrome; stiffness, spasms and involuntary movements of the muscles
- Severe eye pain and decreased or blurred vision
- Vertigo
- Decrease in blood pressure; abnormal, rapid or irregular heartbeat, which could lead to fainting; 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)
- Coughing, wheezing, shortness of breath and a high temperature, which are symptoms of inflammation of the lungs associated with an increase in white blood cells (pulmonary eosinophilia)
- 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); slight changes in blood levels of liver enzymes
- Skin rash, which may lead to severe blistering and peeling of the skin; itching; mild rash
- Unexplained muscle pain, tenderness or weakness (rhabdomyolysis)
- Abnormal breast milk production

Axyven XL sometimes causes unwanted effects that you may not be aware of, such as increases in blood pressure or abnormal heartbeat; slight changes in blood levels or liver enzymes, sodium or cholesterol. More rarely, Axyven XL 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 Axyven XL for a long time.

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Axyven XL

- **KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.**
- Do not use Axyven XL after the expiry date (Exp) which is stated on the carton and blister labels. The expiry date refers to the last day of that month.
- Do not store above 30°C.
- Store in the original package in order to protect from moisture.
- If your doctor decides to stop the treatment, return any leftover medicine to the pharmacist. Only keep it if your doctor tells you to.
- If your medicine appears to be discoloured or show any other signs of deterioration, please return to your pharmacist who will advise you further.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Axyven XL contains

The active substance is venlafaxine. Each prolonged-release tablet contains 225mg venlafaxine (as hydrochloride).

The other ingredients are **Core:** mannitol (E421), povidone K-90, macrogol 400, microcrystalline cellulose, colloidal anhydrous silica and magnesium stearate. **Coat:** cellulose acetate, macrogol 400 and Opadry Y 30 18037 (a mixture of hypromellose, lactose monohydrate, titanium dioxide (E171) and triacetin).

What Axyven XL looks like and contents of the pack

Axyven XL are round, biconvex, plain white tablets with a laser hole on one side.

Axyven XL is available in blister packs of 28 tablets.

Manufacturer

Manufactured by:
Laboratorios LICONSA S.A., Avda. Miralcampo No 7, Poligono Industrial Miralcampo, 19200 Azuqueca de Henares (Guadalajara), Spain
or
Italfarmaco S.p.A., Viale F. Testi, 330, 20126 Milan, Italy.

Procured from within the EU and repackaged by:
Doncaster Pharmaceuticals Group Ltd., Kirk Sandall, Doncaster, DN3 1QR.

Product Licence holder:
Landmark Pharma Ltd., 7 Regents Drive, Prudhoe, Northumberland, NE42 6PX.

PL No: 21828/0608

POM

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**Blind or partially sighted?
Is this leaflet hard to see or read?
Call +44 (0) 1302 365000
(Regulatory)**

**Please be ready to give the following information:
Product name:
Axyven XL 225mg
prolonged-release tablets
Reference No: 21828/0608**