

Package leaflet - Information for the user

Sivion XL 225mg Prolonged-Release Tablets

Venlafaxine hydrochloride

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
- Your medicine is called Sivion XL 225mg Prolonged-Release Tablets but will be referred to as Sivion XL throughout this leaflet.

What is in this leaflet:

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

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

Sivion XL contains the active substance venlafaxine. Sivion 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 not fully understood how antidepressants work, but they may help by increasing the levels of serotonin and noradrenaline in the brain.

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

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

Warnings and Precautions

Talk to your doctor or pharmacist **before** taking Sivion XL:

- If you use other medicines that taken together with Sivion XL could increase the risk of developing serotonin syndrome (see the section "Other medicines and Sivion 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 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 history of bleeding disorders (tendency to develop bruises or a tendency to bleed easily) or if you are taking other medicines that may increase the risk of bleeding e.g. warfarin (used to prevent blood clots), 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.

Sivion 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.

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

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. These thoughts may also occur when your dose is decreased or during discontinuation of treatment with Sivion XL.

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

Sexual problems

Medicines like Sivion XL (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

Sivion 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 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 Sivion XL. 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 Sivion 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 Sivion 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 Sivion 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 Sivion 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 amphetamines (used to treat attention deficit hyperactivity disorder (ADHD), narcolepsy and obesity)
 - Medicines containing linezolid, an antibiotic (used to treat infections)
 - Medicines containing moclobemide, an MAOI (used to treat depression)
 - Medicines containing sibutramine (used for weight loss)
 - Medicines containing opioids (e.g., buprenorphine, 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.

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 Sivion 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)

Sivion XL with food, drink and alcohol

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

Do not drink alcohol while being treated with Sivion XL. Concomitant use with alcohol can lead to extreme tiredness and unconsciousness and can make your symptoms of depression and other conditions, such as anxiety disorders worse.

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 Sivion 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 Sivion 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 take Sivion XL 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 Sivion XL so they can advise you.

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.

Sivion XL 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 this medicine.

Driving and using machines

Do not drive or use any tools or machines until you know how this medicine affects you.

Sivion XL contains lactose

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 Sivion 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
(Continued overleaf)

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 Sivion 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.

Sivion XL 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 different.

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

If you take more Sivion XL than you should

Call your doctor or pharmacist immediately if you take more of this medicine than the amount prescribed by your doctor.

Overdose can be life-threatening, especially with concomitant use of alcohol and/or certain medicines (see "Other medicines and Sivion XL").

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

If you stop taking Sivion 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 Sivion 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 this medicine, especially when it 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, nervousness, agitation, confusion, ringing in the ears, tingling or rarely electric shock sensations, weakness, sweating, seizures, or flu-like symptoms, problems with eyesight and increase in blood pressure (which can cause headache, dizziness, ringing in the ears, sweating, etc.)

Your doctor will advise you on how you should gradually discontinue Sivion XL 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 Sivion 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, mouth, tongue, throat, hands, or feet, and/or a raised itchy 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)
- 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.
- Severe rash, which may lead to severe blistering and peeling of the skin.
- Unexplained muscle pain, tenderness or weakness. This may be 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 are 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 Sivion XL, if you stop taking Sivion XL")
- 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 a tablet in your stools after taking Sivion XL. As the tablet travels the length of your gastrointestinal tract, Sivion XL 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 Sivion XL has been absorbed.

Other side effects that may occur

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

- Dizziness; headache; drowsiness
- Insomnia
- Nausea; dry mouth; constipation
- 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; agitation; nervousness; abnormal dreams
- Tremor, a sensation of restlessness or an inability to sit or stand still; pins and needles; altered taste sensation; increased muscle tonus
- 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)
- Fast heartbeat; palpitations
- Increase in blood pressure; flushing
- Shortness of breath; yawning
- Vomiting; diarrhoea
- Mild rash; itching
- 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
- Weight gain; weight loss
- Increased cholesterol

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; impaired coordination and balance
- Feeling dizzy (particularly when standing up too quickly); decrease in blood pressure
- Vomiting blood, black tarry stools (faeces) or blood in stools; which can be a sign of internal bleeding
- Sensitivity to sunlight; bruising; abnormal hair loss
- Inability to control urination
- Stiffness, spasms and involuntary movements of the muscles
- Slight changes in blood levels of liver enzymes

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

- Seizures or fits
- Coughing, wheezing and shortness of breath which may be accompanied by a high temperature
- Disorientation and confusion often accompanied by hallucination (delirium)
- Excessive water intake (known as SIADH)
- Decrease in blood sodium levels
- 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)

- Prolonged bleeding, which may be a sign of reduced number of platelets in your blood, leading to an increased risk of bruising or bleeding
- Abnormal breast milk production
- 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)

Frequency 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 Sivion XL)
- Aggression
- Vertigo
- Heavy vaginal bleeding shortly after birth (postpartum haemorrhage), see "Pregnancy and breast-feeding" in section 2 for more information

Sivion 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, Sivion 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 Sivion XL 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 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 Sivion XL

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

Do not use Sivion XL after the expiry date which is stated on the packaging.

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.

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.

Do not use if any signs of deterioration are seen.

6. Contents of the pack and other information

What Sivion 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, cellulose microcrystalline, colloidal anhydrous silica, magnesium stearate.

Coat: cellulose acetate, macrogol 400, hypromellose, lactose monohydrate, titanium dioxide (E171), triacetin.

What Sivion XL looks like and contents of the pack

White round tablets, plain on one side with a laser hole on the reverse.

Sivion XL is available in a pack size of 30 tablets.

PL holder:

Manx Pharma Ltd, Unit 2, Bosworth Avenue, Tournament Fields, Warwick, CV34 6UQ, UK

PL 15833/0066 POM

Procured from within the EU.

Manufacturer:

Laboratorios LINCOSA S.A. Avda. Miralcampo, No 7, Poligono Industrial Miralcampo

19200 Azuqueca de Henares (Guadalajara), SPAIN

To request a copy of this leaflet in large print,

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MANX
Pharma

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