VI.2 Elements for a Public Summary

[Product name] 37.5 mg prolonged-release capsules, hard
[Product name] 75 mg prolonged-release capsules, hard
[Product name] 150 mg prolonged-release capsules, hard
[Product name] 225 mg prolonged-release capsules, hard

VI.2.1 Overview of disease epidemiology

Major Depressive Disorder (MDD)

Depression is different from feeling sad or down every now and then. People with depression constantly feel sad, with lack of energy, and have difficulty enjoying routine daily activities. Other symptoms of depression include: changes in sleeping habits such as sleeping poorly or sleeping more than usual, losing interest in typically pleasurable activities, not eating as much or eating more etc. Depression is a very common condition that affects around one in every five people. Many factors may cause depression, including the genetic factors, brain chemistry, and environmental factors (e.g. stress). Some of the risk factors are traumatic experience(s), family history, alcohol abuse or abuse of illicit drugs and chronic conditions (e.g. cancer).

Generalized Anxiety Disorder (GAD)
Generalized anxiety disorder is a severe, ongoing anxiety condition that interferes with day-to-day activities that occurs in both children and adults. GAD is similar in some ways to panic disorder, obsessive-compulsive disorder and other types of anxiety. In many cases, GAD occurs along with other anxiety or mood disorders. The symptoms of GAD are prolonged excessive and difficult to control anxiety and worry, which can cause restlessness, fatigue, concentration difficulties or memory impairment, irritability, muscle tension or sleep disorders. GAD develops in about 1 in 50 people at some stage in their life and affects twice as many women as men. It usually develops in a person's 20s, but is frequently recognised in elderly as well.

Social Anxiety Disorder (SAD)
Social anxiety disorder (social phobia) is a condition in which people have irrational anxiety, fear, self-consciousness and embarrassment around everyday social interactions. Comfort levels in social situations vary from individual to individual due to personality traits and life experiences. Some people are naturally reserved and others are more outgoing. What sets SAD apart from everyday nervousness is that its symptoms are much more severe and may actually cause patients to avoid everyday social interactions. Risk factors include family history, past negative experiences or having a condition which marks a person (e.g. facial abnormalities).

Panic Disorder

Panic disorder is a condition in which people experience regular repeated, often unpredictable, panic attacks. A panic attack is a sudden episode of intense fear that may trigger severe physical reactions, occuring without real danger or apparent cause. Many people have just one or two panic attacks in their lifetimes, perhaps during stressful situation ends, but do not experience persistent attacks.

VI.2.2 Summary of treatment benefits

[product name] contains the active substance venlafaxine.

[product name] 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.

[product name] is a treatment for adults with depression. It 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.

VI.2.3 Unknowns relating to treatment benefits

The efficacy and safety of venlafaxine for other indications in children and adolescents under the age of 18 have not been established.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Suicidal thoughts	Depression, the condition vanlafaxine may be used to treat, in itself carries the risk of suicidal thoughts, self-harm and suicide. Close supervision of patients, in particular those at high risk, should accompany venlafaxine therapy Some people may be more at risk of having suicidal thoughts or actions, especially if they have (or have a family history of) bipolar illness (also called manic-depressive illness) or if they have had suicidal thoughts in the past. Young adults are also at a higher risk.	Monitoring for early symptoms (e.g. sudden changes in mood, behaviors, thoughts, or feelings), especially when venlafaxine e is started or when the dose is changed. Venlafaxine is not recommended for use in children and adolescents.
Abnormal levels of a chemical (serotonin) in the brain (Serotonin Syndrome)	Abnormal levels of a chemical (serotonin) in the brain may occur with venlafaxine when taken with other medicines having serotonin-like properties. Some symptoms include: restlessness, increase in blood pressure, hallucinations (seeing and hearing things that are not real), diarrhoea, loss of coordination, coma, fast heart beat, nausea, increased body temperature, vomiting, muscle stiffness and/or confusion.	Avoid concomitant use of medicines that affect serotonin and monitoring for early symptoms of serotonin syndrome in patients at risk. Patients should inform their doctor about all medicines they are taking (inluding OTC products).
Abnormality in the heart's electrical system	QT prolongation is an abnormality in the heart's electrical system. Although it does not produce	Avoid the use of venlafaxine in patients with heartc conduction

(QT prolongation/ Torsade de Pointes (TdP))	symptoms, it sometimes progresses to Torsade de Pointes (very fast, abnormal and dangerous heart rhythm). Torsades de pointes may cause persistent palpitations (a sensation of fluttering or pounding in the chest or loss of consciousness) and can be fatal.	problems. Patients should undergo a prompt medical evaluation for any palpitations (feeling of the heart fluttering or racing).
Seizure (Convulsion)	Seizures are uncommon with velafaxine, but can occur when it isare combined with other medicines that increase the risk of seizures.	Avoid the use of venlafaxine with medicines known to trigger seizures. Patients should inform their doctor about all medicines they are taking (inluding OTC products).
Low sodium level in the blood (Hyponatraemia/SIADH)	Venlafaxine can cause low sodium levels in the blood. Mildly low levels may not cause any symptoms. If severe, symptoms can occur including: headache, difficulty concentrating, memory changes, confusion, weakness and unsteadiness on the feet. In very severe cases, symptoms can also include: hallucinations (seeing or hearing things that are not real), fainting, seizures, coma, and even death.	Monitor for early symptoms, especially in elderly patients, in patients taking diuretics (fluid tablets), and in dehydrated patients.
Abnormal bleeding	Venlafaxine may increase the risk of bleeding, especially from the upper gastrointestinal tract. Taking aspirin, or blood thinners (e.g. warfarin) may increase the risk of bleeding.	Monitor for early symptoms. Patients should be instructed to report any signs of bleeding immediatelly (e.g. bruising).
Aggression	Venlafaxine may lead to agitation and aggression in depressed patients.	Monitor for early symptoms. Venlafaxine should be used cautiously in patients with a history of aggression.
Symptoms occuring when velafaxine is stopped (Withdrawal symptoms)	Side effects may occur when venlafaxine is stopped (discontinuation symptoms), especially when therapy is stopped suddenly. Some of these side effects may include: dizziness, anxiety, nausea, abnormal dreams, headache, tiredness, irritability, sweating, sleeping problems, diarrhoea, seizures.	Venlafaxine should not be discontinued suddenly. Patients should never stop venlafaxine without first talking to their doctor. If the medication is discontinued, close monitoring is recommended.

Abnormal elevated or irritable mood (Mania/hypomania)	Mania is a condition in which a person feels and acts very excited, irritable or agitated for a prolonged period. In some patients, it may show up primarily as immobility and unresponsiveness to the surrounding world. Milder degrees of mania are sometimes called 'hypomania'.	Monitor for early symptoms; patient should contact a health care provider. Venlafaxine should be used cautiously in patients with a history or family history of bipolar disorder.
Increased blood pressure / increased heart rate	Dose-related increases in blood pressure have been commonly reported with venlafaxine. In some cases, severely elevated blood pressure, requiring immediate treatment, has been reported in postmarketing experience. Increases in heart rate can occur, particularly with higher doses.	Blood pressure and heart rate monitoring are recommended for patients taking venlafaxine. For patients with previous diagnosis of high blood pressure, the blood pressure should be controlled before starting treatment with venlafaxine.
Increased serum cholesterol	Elevations in lipids, including cholesterol and triglycerides, were observed in clinical trials.	Monitor lipid levels, especially during long-term treatment.
Severe cutaneous adverse reactions (SCAR) including Stevens-Johnson syndrome (SJS), Erythema multiforme (EM) and toxic epidermal necrolysis (TEN)	Stevens-Johnson syndrome and toxic epidermal necrolysis are severe diseases characterized by extensive blisters, high fever, sloughing and painful skin. If very severe, they can sometimes be life threatening or even fatal.	Monitoring for early symptoms.
Increase of the pressure in the eye (Narrow angle glaucoma)	Narrow angle glaucoma is a type of glaucoma, which an increase of the pressure in the eye that can result in optic nerve damage and partial or complete loss of vision. Some possible symptoms of narrow angle glaucoma include eye pain (sometimes accompanied by nausea and vomiting), sudden onset of vision problems (which may be more noticeable in low light), blurred vision, halos around lights and reddening of the eye.	Monitor for early symptoms. Patients should be instructed to report on any eye events.
Risk of persistent pulmonary hypertension in neonates (PPHN)	Epidemiological data have suggested that the use of the group of drugs, that venlafaxine belongs to, in pregnancy (particularly in late pregnancy) may increase the risk of persistent pulmonary hypertension in the newborn (PPHN) (high blood pressure that	Venlafaxine must only be administered to pregnant women if the expected benefits outweigh any possible risk.

	affects the arteries in lungs and the right side of the heart). This risk cannot be ruled out with venlafaxine.	
Use of venlafaxine with other medicines that can increase the levels of serotonin, a substance in the body (Interactions with other drugs: Monoamine oxidase inhibitors (MAOIs), Serotonergic agents)	When more than one antidepressant is taken, increase in the levels of serotonin in the body may rise. Some symptoms include: restlessness, increase in blood pressure, hallucinations (seeing and hearing things that are not real), diarrhoea, loss of coordination, coma, fast heart beat, nausea, increased body temperature, vomiting, muscle stiffness and/or confusion.	Avoid concomitant use of medicines that affect serotonin and monitoring for early symptoms of serotonin syndrome in patients at risk. Patients should inform their doctor about all medicines they are taking (inluding OTC products).

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Ischemic cardiac events	Heart events occuring due to insufficient blood supply to the heart may occur with venlafaxine use. Causal realtionship has so far not been established.
Diabetes	In patients with existing diabetes, treatment with venlafaxine may alter blood sugar control. Insulin and/or oral antidiabetic drug dosage may need to be adjusted.
Use in pregnancy and lactation	There are no adequate data from the use of venlafaxine in pregnant women. As with other drugs of the same class, discontinuation symptoms may occur in the newborns if venlafaxine is used until or shortly before birth. Some newborns exposed to venlafaxine late in the third trimester have developed complications requiring tube feeding respiratory support or prolonged hospitalisation. Such complications can arise immediately upon delivery. The following symptoms may be observed in neonates if the mother has used venlafaxine in late in pregnancy: irritability, tremor, hypotonia, persistent crying, and difficulty in sucking or in sleeping. In the majority of cases, these complications are observed immediately or within 24 hours after partus. Venlafaxine and its active metaboliteare excreted in breast milk. There have been reports of breast-fed infants who experienced crying, irritability, and abnormal sleep patterns. Symptoms consistent with venlafaxine drug discontinuation have also been reported after stopping breast-feeding. A risk to the suckling child cannot be excluded.

Missing information

Risk	**What is known**

Use in pediatric patients	Venlafaxine is not recommended for use in children and adolescents. Controlled clinical studies in children and adolescents with major depressive disorder failed to demonstrate efficacy and do not support the use of venlafaxine in these patients. The efficacy and safety of venlafaxine for other indications in children and adolescents under the age of 18 have not been established.
Use in elderly patients	Caution should be exercised in treating the elderly (e.g. due to the possibility of kidney impairment). The lowest effective dose should always be used, and patients should be carefully monitored when an increase in the dose is required.
Use in patients with severe hepatic impairment	There are limited data in patients with severe liver impairment. Caution is advised, and a dose reduction by more than 50 % should be considered. The potential benefit should be weighed against the risk in the treatment of patients with severe liver impairment.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post-authorisation studies have been imposed or are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable.