# VENXOR

VIDIAxx-PC

## DESCRIPTION
Peach mottled, shield shape uncoated tablet, bevel-edged, flat faces and a break-bar on one face.

## COMPOSITION
Each tablet contains:
Venlafaxine HCl equivalent to Venlafaxine 50 mg.

## ACTIONS AND PHARMACOLOGY
Venlafaxine has virtually no affinity for rat brain muscarinic, histaminergic or adrenergic receptors *in vitro*. Pharmacologic activity at these receptors may be related to various side effects seen with other antidepressant drugs, such as anticholinergic, sedative and cardiovascular effects. Venlafaxine does not possess monoamine oxidase (MAO) inhibitory activity.

## PHARMACOKINETICS
Venlafaxine is well absorbed and undergoes extensive first-pass metabolism. Mean peak plasma concentrations of venlafaxine range from approximately 33 to 172 ng/ml after 25 to 150 mg single doses, and are reached in approximately 2.4 hours. Venlafaxine is extensively metabolised in the liver. O-desmethylvenlafaxine (ODV) is the major active metabolite of venlafaxine.

## INDICATIONS
Venlafaxine is indicated for the treatment of depression, including depression associated with anxiety, in both hospitalized patients and outpatients. For prevention of relapse of an episode of depression or for prevention of the recurrence of new depressive episodes.

## CONTRAINDICATIONS
- Known hypersensitivity to venlafaxine or any other component of the product.
- Concomitant use of venlafaxine with monoamine oxidase inhibitors.
- Venlafaxine should not be used in patients with an identified very high risk of a serious cardiac ventricular arrhythmia (e.g. those with a significant left ventricular dysfunction, NYHA Class III/IV) or uncontrolled hypertension.
- Venlafaxine should not be used in children and adolescents under the age of 18 years with Major Depressive Disorder.

## PRECAUTIONS
**Suicidality in Children and Adolescents**
- Antidepressant increases the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders.
- Anyone considering the use of antidepressant in a child or adolescent for any clinical use must balance the risk of increased suicidality with the clinical need.
- Patients who are started on therapy should be observed closely for clinical worsening, suicidality or unusual changes in behavior.
- Families and caregivers should be advised to closely observe the patient and to communicate with the prescriber.
- A statement regarding whether the particular drug is approved for any pediatric indication (s) and, if so.
- This product is not indicated for paediatric use.

## PREGNANCY AND LACTATION
Not recommended in pregnancy and lactation. Venxor tablet should not be used during pregnancy unless clearly necessary. There is evidence to suggest that venlafaxine and its metabolite, ODV are distributed into breast milk and may cause unwanted effects in the nursing infant. Thus, decision should be made whether or not to breast-feed or to discontinue venlafaxine.

## INTERACTION WITH OTHER MEDICAMENTS
- **Monoamine Oxidase Inhibitors (MAOI)**
  - Irreversible non-selective MAOIs: Venlafaxine must not be used in combination with irreversible non-selective MAOIs. Venlafaxine must not be initiated for at least 14 days after discontinuation of treatment with an irreversible non-selective MAOI. Venlafaxine must be discontinued for at least 7 days before starting treatment with an irreversible non-selective MAOI.
  - Reversible, selective MAO-A inhibitor (moclobemide): Due to the risk of serotonin syndrome, the combination of venlafaxine with a reversible and selective MAOI, such as moclobemide, is not recommended. Following treatment with a reversible MAO-inhibitor, a shorter withdrawal period than 14 days may be used before initiation of venlafaxine treatment. It is recommended that venlafaxine should be discontinued for at least 7 days before starting treatment with a reversible MAOI.
  - Reversible, non-selective MAOI (linezolid): The antibiotic linezolid is a weak reversible and non-selective MAOI and should not be given to patients treated with venlafaxine.

    Severe adverse reactions have been reported in patients who have recently been discontinued from an MAOI and started on venlafaxine, or have recently had venlafaxine therapy discontinued prior to initiation of an MAOI. These reactions have included tremor, myoclonus, diaphoresis, nausea, vomiting, flushing, dizziness, and hyperthermia with features resembling neuroleptic malignant syndrome, seizures, and death.

- **Serotonin syndrome:** As with other serotonergic agents, serotonin syndrome, a potentially life-threatening condition, may occur with venlafaxine treatment, particularly with concomitant use of other agents that may affect the serotonergic neurotransmitter system (including triptans, SSRIs, SNRIs, lithium, sibutramine, tramadol, or St. John's Wort [Hypericum perforatum], fentanyl and its analogues, tramadol, dextromethorphan, tapentadol, pethidine, methadone and pentazocine), with medicinal agents that impair metabolism of serotonin (such as MAOIs e.g. methylene blue), with serotonin precursors (such as tryptophan supplements) or with antipsychotics or other dopamine antagonists.

  If concomitant treatment with venlafaxine and an SSRI, an SNRI or a serotonin receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of venlafaxine with serotonin precursors (such as tryptophan supplements) is not recommended.

- **CNS-active substances:** The risk of using venlafaxine in combination with other CNS-active substances has not been systematically evaluated. Consequently, caution is advised when venlafaxine is taken in combination with other CNS-active substances.

- **Ethanol:** Venlafaxine has been shown not to increase the impairment of mental and motor skills caused by ethanol. However, as with all CNS-active substances, patients should be advised to avoid alcohol consumption.

- **Effect of other medicinal products on venlafaxine**
  - Ketoconazole (CYP3A4 inhibitor): Higher AUC of venlafaxine and O-desmethylvenlafaxine occurred in extensive and poor metaboliser after administration of ketoconazole. Concomitant use of CYP3A4 inhibitors (e.g., atazanavir, clarithromycin, indinavir, itraconazole, voriconazole, posaconazole, ketoconazole, nelfinavir, ritonavir, saquinavir, telithromycin) and venlafaxine may increase levels of venlafaxine and O-desmethylvenlafaxine. Therefore, caution is advised if a patient's therapy includes a CYP3A4 inhibitor and venlafaxine concomitantly.

- **Effect of venlafaxine on other medicinal products**
  - Lithium: Serotonin syndrome may occur with the concomitant use of venlafaxine and lithium (see Serotonin syndrome).
  - Diazepam: Venlafaxine has no effects on the pharmacokinetics and pharmacodynamics of diazepam and its active metabolite, desmethyldiazepam. Diazepam does not appear to affect the pharmacokinetics of either venlafaxine or O-desmethylvenlafaxine. It is unknown whether a pharmacokinetic and/or pharmacodynamic interaction with other benzodiazepines exists.

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- ***Imipramine:*** Venlafaxine did not affect the pharmacokinetics of imipramine and 2-OH-imipramine. There was a dose-dependent increase of 2-OH-desipramine AUC by 2.5 to 4.5-fold when venlafaxine 75 mg to 150 mg daily was administered. Imipramine did not affect the pharmacokinetics of venlafaxine and O-desmethylvenlafaxine. The clinical significance of this interaction is unknown. Caution should be exercised with co-administration of venlafaxine and imipramine.
- ***Haloperidol:*** Co-administration with haloperidol has shown a decrease in total oral clearance, a increase in AUC, an increase in Cmax, but no change in half-life for haloperidol. This should be taken into account in patients treated with haloperidol and venlafaxine concomitantly. The clinical significance of this interaction is unknown.
- ***Risperidone:*** Venlafaxine increased the risperidone AUC by 50%, but did not significantly alter the pharmacokinetic profile of the total active moiety (risperidone plus 9-hydroxyrisperidone). The clinical significance of this interaction is unknown.
- ***Metoprolol:*** Concomitant administration of venlafaxine and metoprolol to healthy volunteers for both medicinal products resulted in an increase of plasma concentrations of metoprolol by approximately 30-40% without altering the plasma concentrations of its active metabolite, α-hydroxymetoprolol. The clinical relevance of this finding in hypertensive patients is unknown. Metoprolol did not alter the pharmacokinetic profile of venlafaxine or its active metabolite, O-desmethylvenlafaxine. Caution should be exercised with co-administration of venlafaxine and metoprolol.
- ***Indinavir:*** Indinavir has shown a decrease in AUC and a decrease in Cmax for indinavir. Indinavir did not affect the pharmacokinetics of venlafaxine and O-desmethylvenlafaxine. The clinical significance of this interaction is unknown.

## MAIN SIDE/ADVERSE EFFECTS

- Venlafaxine is generally well-tolerated, the occurrence of most of these adverse events was dose-related, and the majority of them decreased in intensity and frequency over time. They generally did not lead to cessation of treatment.
- The most commonly observed adverse events associated with the use of venlafaxine, and which occurred more frequently than those which were associated with placebo were: nausea, vomiting, insomnia, dry mouth, somnolence, headache, hypertension, dizziness, constipation, sweating, nervousness, vision disturbances (including abnormal accommodation and blurred vision), asthenia and sexual dysfunction (including abnormal ejaculation/orgasm, anorgasmia).
- The incidence that occurred rare includes dyspnea, edema, itching skin rash, mania or hypomania, menstrual changes, orthostatic hypotension, seizures, trismus, urinary effects (including impaired urination, urinary frequency, urinary incontinence, or urinary retention).

## OVERDOSE

- **Clinical features:** Agitation, electrocardiogram (ECG) changes, specifically QTc prolongation, lethargy, paresthesia, seizures, sinus tachycardia, somnolence, tremor.
- **Treatment of overdosages:** There is no specific antidote for venlafaxine. Treatment is essentially symptomatic and supportive.

## DOSAGE AND ADMINISTRATION

For oral use.
The recommended starting dose of immediate-release venlafaxine is 75 mg/day in two or three divided doses taken with food.

When required, the venlafaxine dosage can be increased in increments of up to 75 mg/day, at intervals of no less than 4 days. The venlafaxine dose can be titrated up to 225 mg/day in moderately depressed patients and 375 mg/day for severely depressed patients. The maximum recommended dosage of venlafaxine is 375 mg/day, generally administered in three divided doses. Usually, the dosage for prevention of relapse or for the prevention of recurrence of a new episode is similar to that used during initial treatment.

Patients should be regularly reassessed in order to evaluate the benefit of long-term therapy. Dose tapering is recommended when discontinuing venlafaxine therapy. Tapering over at least a two-week period is recommended if venlafaxine has been used for more than 6 weeks. The period required for tapering may depend on the dose, duration of therapy, and the individual patient.

- **Use in Patients with Renal Impairment:** The total daily dose of venlafaxine must be reduced by 25-50% for patients with renal impairment with a glomerular filtration rate (GFR) of 10-70 mL/min. The total daily dose of venlafaxine must be reduced by 50% in hemodialysis patients. Administration must be withheld until the dialysis session is completed.
- **Use in Patients with Hepatic Impairment:** The total daily dose of venlafaxine must be reduced by 50% in patients with moderate hepatic impairment. Reductions of more than 50% may be appropriate for some patients.
- **Use in Children:** There is insufficient experience with the use of venlafaxine in patients less than 18 years of age.
- **Use in Elderly Patients:** No specific dosage adjustments of venlafaxine are recommended based on patient age.
- **Maintenance / Continuation / Extended Treatment:** The physician should periodically reevaluate the usefulness of long-term venlafaxine treatment for the individual patient. It is generally agreed that acute episodes of major depression require several months or longer of sustained pharmacologic therapy. Whether the dose of antidepressant needed to induce remission is identical to the dose needed to maintain and/or sustain euthymia is unknown.

Note: The information given here is limited. For further information consult your doctor or pharmacist.

Storage: Store below 25°C. Protect from light and moisture.
Presentation/Packing: Blister Pack of 1 x10's, 3 x 10's , 10 x10's

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Revision date: September 2014.

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