

**HIGH DOSE VENLAFAXINE (300 mg/day or over)
Primary Care Information Leaflet**

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Further information for this guideline is available from:

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Approved Indication

Venlafaxine is included in the Sunderland Joint Formulary for use in patients who are not responding adequately to first line treatments for major depressive disorder including depression accompanied by anxiety. Following an initial response venlafaxine is indicated for the prevention of relapses of the initial episode of depression or for the prevention of the recurrence of new episodes. Resistant depression may require venlafaxine treatment at doses at or above 300mg daily. (RAG status green plus for doses of 300mg daily or over)

Background

Venlafaxine is a Serotonin/Noradrenaline Reuptake Inhibitor (SNRI) antidepressant. The licensed dose is 75mg daily initially, increased in steps of 75mg to a maximum licensed dose of 375mg daily for depression. **Doses higher than 375mg may be prescribed, however this is done on an off-label basis.**

Treatment with high dose venlafaxine (300 mg/day or over) should only be initiated on the advice of a mental health specialist

Monitoring

Baseline blood pressure (BP) and heart rate will have been taken before starting venlafaxine in any new patient. BP should be monitored regularly, especially where doses used are over 225mg/day. There are no guidelines available as to specific frequency of monitoring, but based on available studies where dose-related increases have occurred, it has been suggested BP and heart rate is monitored at 4 weeks, 8 weeks and 12 weeks and then if stable 6 monthly thereafter for doses over 225mg/day.

For patients who experience a sustained increase in blood pressure while receiving venlafaxine, either dose reduction or gradual discontinuation (over at least four weeks), or treatment of the elevated blood pressure as clinically indicated should be considered. Ideally this should be discussed with the specialist team if the patient is still under their care.

Cautions

- Patients with increased risk factors for suicide should be carefully evaluated for the presence of worsening of suicide related behaviour and a limited number of tablets should be provided to reduce the risk of overdose. A maximum of 2 weeks supply should be considered in these patients at initiation of treatment, during any dosage adjustment and until improvement occurs.

- Venlafaxine should be used in caution in patients with established cardiac disease that may increase the risk of ventricular arrhythmias.
- Due to reports of mydriasis, patients with raised intra-ocular pressure or at a risk of narrow angle glaucoma should be monitored closely.
- SSRI and dual action antidepressants have been reported to cause bleeding disorders in some patients. Caution is advised in patients predisposed to bleeding due to factors such as age, underlying medical conditions or concomitant medications. Particular caution is warranted in older people taking non-steroidal anti-inflammatory drugs or aspirin.
- In patients with diabetes, treatment with venlafaxine may alter glycaemic control. Insulin and/or oral antidiabetic dosage may need to be adjusted.
- Convulsions may occur with venlafaxine therapy. As with all antidepressants, venlafaxine should be introduced with caution in patients with a history of epilepsy.
- Dual action antidepressants should not be used in patients with a diagnosis of bipolar disorder as there is a higher risk of mania.

Contra-indications

- Known hypersensitivity to venlafaxine or any other component of the product.
- Concomitant use of venlafaxine with monoamine oxidase inhibitors.
- An identified very high risk of a serious cardiac ventricular arrhythmia (e.g. those with a NYHA Class III/IV left ventricular failure, a recent history of MI) or uncontrolled hypertension.
- Children and adolescents under the age of 18 years with Major Depressive Disorder.

Withdrawal

Venlafaxine, in common with paroxetine, is associated with a greater likelihood of developing a withdrawal reaction following discontinuation. Therefore the dose should be tapered gradually over at least four weeks as tolerated by the patient.

Discontinuation reaction symptoms may arise within a few days of dose reduction or omission and typically include symptoms such as electric shock sensations, paraesthesia, 'flu-like symptoms', light headedness and dizziness exacerbated by movement, insomnia, excessive (vivid) dreaming, irritability and crying spells, anxiety and agitation.

Side-effects

Commonly reported adverse effects (incidence > 1/1000) include:

Constipation, nausea, asthenia, headache, dizziness, dry mouth, insomnia, nervousness, somnolence, sexual dysfunction, sweating (including night sweats), anorexia, appetite decreased, diarrhoea, dyspepsia, vomiting, hypertension, palpitations, abdominal pain, chills, pyrexia, serum cholesterol increased particularly with prolonged administration and possibly with higher doses, weight gain or loss, arthralgia, myalgia, abnormal dreams, agitation, anxiety, confusion, hypertonia, paraesthesia, tremor, urinary frequency, menstrual cycle disorders, dyspnoea, yawning, pruritus, rash, abnormal vision/ accommodation, mydriasis, tinnitus.

Drug Interactions

- Serotonergic drugs: Based on the potential for serotonergic syndrome, caution is advised when venlafaxine is co-administered with drugs that may affect the serotonergic neurotransmitter systems (e.g. triptans, SSRIs, tramadol or lithium). It should be noted that, although lithium should be used with caution with venlafaxine, these drugs are often used in combination.

- MAOIs: venlafaxine should not be started until 2 weeks after stopping MAOIs, avoid MAOIs for one week after stopping venlafaxine.
- Haloperidol- haloperidol serum levels increased.
- Potent CYP3A4 inhibitors (e.g. azole antifungals, erythromycin)- potential for increased venlafaxine levels.
- Warfarin- potentiation of anticoagulant effect reported following the addition of venlafaxine.

Communication with Mental Health Specialist Team, if still involved

Contact the specialist team if any of the following arise:

- Sudden deterioration in mood/functioning
- Patient intolerance or adverse side effects to medication
- Non-concordance with medication
- Changes in prescribing circumstances e.g. initiation of potentially interacting medication (see SPC/BNF)
- Withdrawal of venlafaxine.

NHS Cost

Prices accessed from Drug Tariff, September 2016

Venlafaxine tablets 37.5mg	Pack of 56	£2.04
Venlafaxine tablets 75mg	Pack of 56	£2.35
Venlafaxine MR 75mg tablets	Pack of 30	£11.20
Venlafaxine MR 150mg tablets	Pack of 30	£18.70

Other information

See the manufacturer's SPC or BNF for more detailed prescribing information.