

## North of Tyne and Gateshead Area Prescribing Committee High Dose Venlafaxine - Information leaflet for primary care

### Approved Indication

Venlafaxine is included in the North of Tyne and Gateshead Formulary as a Green Plus drug 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.

### 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

- Pre-treatment - Baseline blood pressure (BP) and heart rate
- Monitor BP regularly, especially doses > 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
- 12 weeks and then
- 6 monthly if stable thereafter for doses over 225mg/day

Blood pressure and heart rate should also be reviewed periodically following dose changes.

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)
- Similar to other serotonergic agents, venlafaxine may be associated with the development of serotonin syndrome, symptoms of which include mental status changes, autonomic instability, neuromuscular irregularities and/or gastric symptoms.
- Cases of hyponatraemia and/or the Syndrome of Inappropriate Antidiuretic Hormone (SIADH) secretion may occur with venlafaxine. Elderly patients, patients taking diuretics, and patients who are otherwise volume-depleted may be at greater risk of this event.
- Clinically relevant increases in serum cholesterol have been recorded in patients treated with venlafaxine for at least 3 months. Measurement of serum cholesterol levels should be considered during long-term treatment.
- Venlafaxine has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness. It is most likely to occur in the first few weeks of treatment and further dose increases may exacerbate the condition.

### **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. The risk of withdrawal symptoms may be dependent on several factors, including the duration and dose of therapy and the rate of dose reduction. 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

Common or very common

Abnormal dreams; anorexia; anxiety; asthenia; changes in serum cholesterol; chills; confusion; constipation; difficulty with micturition; dizziness; drowsiness; dry mouth; headache; hypertension; hypertonia; insomnia; menstrual disturbances; mydriasis; nausea; nervousness; palpitation; sensory disturbances; sexual dysfunction; sweating; tremor; vasodilatation; visual disturbances; vomiting; weight changes; yawning

### 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.
- The combination of venlafaxine and alcohol is not advisable, though this statement applies equally to many other CNS active substances.
- The risk of QTc prolongation and/or ventricular arrhythmias is increased with concomitant use of other QTc prolonging agents. Co-administration of such medicinal products should be avoided.

### 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 Part VIIIA Category C Drug Tariff, May 2017

Venlafaxine tablets 37.5mg	Pack of 56	£1.93
Venlafaxine tablets 75mg	Pack of 56	£2.15
Venlafaxine MR 75mg capsules	Pack of 28	£2.60
Venlafaxine MR 150mg capsules	Pack of 28	£3.90

### Other information

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