Venlafaxine
“Higher-Dose” (300-375mg/day) in Severe Depression
AMBER 2

Information Sheet for Primary Care Prescribers

---

\( ^a \) – venlafaxine <300mg daily is classified GREEN on the Nottinghamshire Joint Formulary

**Background**

In 2006 the Nottinghamshire Area Prescribing Committee (NAPC) approved a Joint Care Guideline (Amber 1) for venlafaxine when used at doses of 300-375mg per day for severe depression following updated prescribing advice issued by the MHRA. In May 2012 the NAPC reviewed the traffic light status of higher-dose venlafaxine and re-classified it as Amber 2 (Specialist Recommendation) with a supporting Prescribing Information Sheet.

**Guidance on use**

The use of venlafaxine at doses at the higher end of its licensed dose range (300-375mg/day) is a treatment option for those patients with severe depression who have only partially responded to lower doses. The titration upwards to doses of 300-375mg per day should only be undertaken on the advice and initial supervision of a specialist within secondary care mental health services following a full psychiatric assessment (Amber 2).

Venlafaxine has a broad range of side-effects similar to those of TCAs and SSRIs. It can increase blood pressure at higher doses, is associated with a high incidence of discontinuation symptoms and is more toxic than the SSRIs in overdose.

Standard-dose venlafaxine (75-225mg daily) is recommended for the treatment of depression in patients who have not responded to adequate trials on two different antidepressants. This would usually be an SSRI followed by a second SSRI, mirtazapine or lofepramine.

---

**In view of the dose-dependant rise in blood pressure it is important to periodically monitor patient’s blood pressure (see below).**

There is evidence that in overdose (greater than 900 mg) venlafaxine is pro-convulsant compared with TCAs and SSRIs and has a higher fatal toxicity index in overdose than SSRIs. Small quantities should be prescribed (max. 1-2 weeks) to patients at risk of over-dosing with consideration to avoid prescribing the highest strength 225mg modified-release formulation.

**Formulations**

Venlafaxine is available as standard-release generic tablets for twice a day administration and a wide range of branded generic modified-release formulations for once daily administration (e.g. Alventa XL, Bonilux XL, Depefex XL, Efexor XL, Foraven XL, Politid XL, Ranfaxin XL, Tifaxin XL, Venax XL, Venlalic XL, Vensir XL, ViePax XL, Winfex XL).

Some modified-release formulations (e.g. Venlalic XL) release venlafaxine through a small hole in the tablet leaving a “ghost” tablet that passes unchanged through the gastrointestinal tract. Patients should be advised and reassured that if they notice the tablet in their stool the dose of venlafaxine has been absorbed.

**Contraindications**

Hypersensitivity to venlafaxine or to any of its excipients. Concomitant treatment with irreversible MAOIs.

**Cautions**
In view of concerns about its effects on the cardiovascular system venlafaxine should only be used in patients with a high risk of a serious cardiac ventricular arrhythmia and patients with uncontrolled hypertension where the benefits outweigh the risks.

Venlafaxine should generally be avoided or used with caution in patients with heart failure, cardiac arrhythmia, left ventricular hypertrophy, previous MI and hypertension\(^4\)\(^5\).

Dosage reductions may be required in patients with hepatic or severe renal impairment (GFR < 30 ml/min).

**Recommended monitoring**

1. A baseline ECG is not required, unless clinically indicated. It should be repeated one week after any dose increase in high-risk patients.
2. Blood pressure (BP) measurement should be performed before starting venlafaxine. If baseline BP is raised (systolic >140mmHg or diastolic >90mmHg) this should be managed in line with current hypertension guidelines. Hypertension should be controlled before starting venlafaxine.
3. Monitor the patient’s blood pressure 4 weeks and 8 weeks after initiation or following any subsequent dose increase and then every 6 months thereafter (every 3 months for patients prescribed above 225mg/day).
4. If there is evidence of a sustained increase in blood pressure compared with baseline the following options can be considered depending on the magnitude of the increase, patient response to treatment, history of non-response to other medication and general medical status: reduce venlafaxine dose, change antidepressant, initiate or alter antihypertensive treatment.

**Drug interactions**

Venlafaxine is metabolised by both CYP2D6 and CYP3A4. Potent CYP2D6 inhibitors (e.g. fluoxetine, paroxetine), potent CYP3A4 inhibitors (e.g. ketoconazole, erythromycin) or drug combinations that inhibit both CYP2D6 and CYP3A4 should only be co-administered when strictly indicated, because of the possibility of clinically important interactions in patients with a ‘poor metaboliser’ phenotype.

Co-administration of medicinal products which may prolong the QT Interval should be avoided.

Combinations of venlafaxine with other antidepressants in treatment-resistant depression (e.g. SSRIs, mirtazapine) should only be undertaken under the supervision of a specialist within secondary care mental health services due to the risk of serotonin syndrome.

**Discontinuation / withdrawal symptoms**

Venlafaxine has a short half-life and is associated with a greater frequency of withdrawal discontinuation reactions than most other antidepressants. The dose should be tapered gradually over a period of about 4 weeks or so, according to the patients need. The 37.5mg tablets are scored allowing doses of 18.75mg to be taken.

Please consult the venlafaxine Summary of Product Characteristics (SPC)\(^3\) for more detailed information. If you require any further advice please contact your local Mental Health Team.

**References**


**Author** - J Lawton, Clinical Pharmacy Services Manager (Nottingham), Nottinghamshire Healthcare NHS Trust