Venlafaxine

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

AMBER 2

Information Sheet for Primary Care Prescribers

(venlafaxine <300mg daily is classified GREEN on the Nottinghamshire Joint Formulary)

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)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 overdose⁴,⁵.

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 or mirtazapine.

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 SSRIs⁴,⁵. 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.

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 hypertension⁴,⁵.

Dose reduction may be required in patients with hepatic or severe renal impairment (GFR< 30 ml/min).
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) for more detailed information. If you require any further advice please contact your local Mental Health Team.

Patient information
For patient information leaflets on venlafaxine and all other psychotropic medicines visit http://www.choiceandmedication.org/nottinghamshirehealthcare/

References
1. NAPC Joint Care Guideline for “High-Dose” venlafaxine (≥300mg daily) in severe depression. Sep 2006. 2. MHRA Updated Prescribing Advice for Venlafaxine. 31.05.2006. 3. Venlafaxine SPCs. 4. NICE CG 90. Depression in Adults (10/2009). 5. NICE CG 91. Depression in adults with a chronic physical health problem (10/2009).

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