

UPDATED PRESCRIBING ADVICE FOR VENLAFAXINE (EFEXOR/EFEXOR XL)

Dear Colleague

I am writing to inform you of updated prescribing advice for the serotonin and noradrenaline reuptake inhibitor (SNRI) antidepressant venlafaxine. The updated advice follows an assessment of the latest safety evidence of venlafaxine, conducted by the Medicines and Healthcare products Regulatory Agency (MHRA), in particular relating to toxicity in overdose.

Background

In December 2004 concerns about potential for cardiotoxicity and toxicity in overdose led to restrictions of venlafaxine to specialist initiation and contraindications in patients with heart disease.

Retrospective analyses from the United Kingdom report the rate of antidepressant overdose deaths per million prescriptions. In these analyses, the rate for venlafaxine is higher than that for SSRIs, but lower than that for tricyclic antidepressants. However, an epidemiological study in patients prescribed antidepressants in the UK shows some evidence that venlafaxine is prescribed to patients with a higher pre-existing suicide risk than patients prescribed SSRIs.

The profile of venlafaxine's toxicity in overdose has not been clearly established. Fatal cardiotoxicity is very rare, but the risk may be increased in those with cardiac disease. Other overdose toxicities include seizures, central nervous system depression, serotonin syndrome and (very rarely) rhabdomyolysis, however the contribution of such reactions to fatal outcomes remains largely unknown. A more detailed report is available on the MHRA website: www.mhra.gov.uk

Updated prescribing advice

The NICE advice that venlafaxine should be reserved as a second-line treatment (after SSRIs) still stands. The following changes have been authorised in line with the review of the evidence:

- **Specialist supervision** (including shared care arrangements) is now only required for initiation of venlafaxine treatment in those severely depressed or hospitalised patients who require doses of 300mg daily, or above.

- **Contra-indications and warnings:** Venlafaxine is contraindicated in patients with an identified high risk of a serious cardiac ventricular arrhythmia. Venlafaxine remains contra-indicated in patients with uncontrolled hypertension.
- The contra-indications for patients with an electrolyte imbalance and the requirement for a baseline ECG have been removed from product information.
- Venlafaxine should be used with caution in patients with established cardiac disease that may increase the risk of ventricular arrhythmias (e.g. recent myocardial infarction).
- Regular measurement of blood pressure is recommended for patients receiving venlafaxine. For patients who experience a sustained increase in blood pressure while receiving venlafaxine, either dose reduction or discontinuation should be considered.
- **Interactions:** Potent CYP3A4 inhibitors (e.g. ketoconazole, erythromycin) or drug combinations that inhibit both CYP3A4 and CYP2D6 should only be co-administered with venlafaxine when strictly indicated, because of the possibility of clinically important interactions in patients with a 'poor metaboliser' phenotype. Specialist supervision is recommended for use of concomitant SSRIs.

Minimising the the risk of overdose

Smaller pack sizes will be available within the coming months. Patients with increased risk factors for suicide should be carefully evaluated for the presence or worsening of suicide related behaviour; a maximum of two weeks supply should be considered for high-risk patients at initiation of treatment, during any dosage adjustment and until improvement occurs.

Action

- Prescribing for new patients should be in line with the updated prescribing advice. An updated, user-tested, patient information leaflet will be available from the manufacturer in the coming months.
- Patients already established on venlafaxine should have a routine treatment review to ensure that their treatment is in line with the latest recommendations (for example cardiac risks, blood pressure and concomitant medicines).

Further information

Further information, including a 'questions and answers' document for patients, is available on the MHRA website www.mhra.gov.uk. The updated product information for venlafaxine is available on the Electronic Medicines Compendium (eMC) website: <http://emc.medicines.org.uk/>

Please report suspected adverse drug reactions to the MHRA and the Commission on Human Medicines (CHM) using the Yellow Card Scheme.

Yours sincerely

Professor Gordon Duff
Chairman, Commission on Human Medicines
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