

ADVICE TO GPs FOR PATIENTS DISCHARGED ON HIGH DOSE VENLAFAXINE (TOTAL DAILY DOSE GREATER THAN 375MG)

High dose venlafaxine:

The Summary of Product Characteristics (SPC) for both XL and plain venlafaxine now states a maximum daily dose of 375mg (an increase for the XL preparation from 225mg).¹

There is limited available evidence for use of venlafaxine above licensed dosage. There are only a small number of studies.

- One is an open label naturalistic case study of 5 patients, (4 patients received 450mg and 1 patient's dose was increased to 600mg during the study). All of these patients fitted the criteria for treatment resistant depression but there was no conclusive evidence that using doses above 375mg had additional benefits as the patients were taking a combination of other psychotropic medications.²
- Another study by Harrison et al looked at the tolerability of high dose venlafaxine. It did not focus on efficacy. 35 patients received doses ranging from 375mg-600mg a day and 35 patients received low dose <375mg. Side effects were reported to be more significant in the high dose group. The authors concluded that this demonstrated tolerability of doses up to 600mg but the numbers were small and rare side effects would have been missed.³

As these studies are small they provide little support for routine use of doses above 375mg.

The United Kingdom Medicines and Healthcare products Regulatory Agency (UK MHRA), recommends that doses above 300mg should only be prescribed under the supervision of or advice of a specialist.⁴

Interactions:

As with other serotonergic agents, the development of serotonin syndrome may occur with venlafaxine treatment, particularly with concomitant use of other serotonergic agents. Where the patient is routinely prescribed any physical medicines that act on the serotonin system e.g. triptans, tramadol, St John's Wort, a discussion should occur between the prescriber and the GP to ensure that these medicines are reviewed.

Serotonin syndrome is a potentially dangerous adverse reaction that is attributed to a toxic hyper-serotonergic state from hyper-stimulation of the brain stem and 5HT1A and 5HT2 receptors. Onset is usually within a few hours of drug or dose changes. Symptoms of serotonin syndrome include and are usually a combination of at least three of the following:

- Mental state changes e.g. confusion, poor co-ordination, hypomania

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- Agitation/Restlessness
- Tremor
- Sweating, fever, shivering
- Gastro intestinal side effects e.g. diarrhoea
- Hypertension
- Tachycardia
- Convulsions

Ensure all other causes have been ruled out e.g. infection, metabolic disturbances, substance misuse or withdrawal.

Monitoring:

The Summary of Product Characteristics of Efexor (venlafaxine) states that all patients should be carefully screened for high blood pressure and pre-existing hypertension should be controlled before initiation of treatment. It also recommends that blood pressure should be reviewed periodically, after initiation of treatment and after each dose increase of venlafaxine.

However there are no guidelines available as to specific frequency of blood pressure monitoring nor is there guidance on specific actions to be taken if blood pressure increases. Locally a decision has been made that if there is an increase of greater than 10mm of mercury or BP reading is above 140 / 90 on two consecutive readings, advice should be sought from the consultant psychiatrist on treatment options. In all cases a risk/benefit discussion needs to take place with the patient, GP and Specialist to decide the safest option with regards to both mental and physical health. 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.

Patient specific monitoring will be detailed in the accompanying clinic letter.

References:

1. Summary of Product Characteristics (Efexor) - accessed 18/04/2011
2. Mbaya P Safety and efficacy of high dose venlafaxine XL in treatment resistant major depression Hum Psychopharmacol Clin Exp 2002 17 335-339 (133112)
3. Harrison CL et al Tolerability of high dose venlafaxine in depressed patients Journal of Psychopharmacology 2004;18/2;200-20
4. UK MHRA. Updated prescribing advice for venlafaxine (Efexor/Efexor XL) 31st May 2006

This leaflet has been produced using information from a number of sources. It is intended to be a summary of available information. For more detailed prescribing information please refer to the summary of product characteristics (www.medicines.org.uk).

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