

# DRUG UPDATE

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## VENLAFAXINE

Venlafaxine should only be started by psychiatrists and medical practitioners with a special interest in mental health for patients whose depression has failed to respond to adequate trials of two other antidepressants. Patients are more likely to stop treatment due to side effects and withdrawal symptoms occur more commonly with venlafaxine than some other SSRIs. It can increase the QT interval so an ECG and blood pressure measurements should be undertaken before starting treatment. Regulatory action based on this advice is subject to an appeal.

### *What is it?*

Venlafaxine (Efexor<sup>®</sup>, Wyeth) is a combined serotonin and noradrenaline re-uptake inhibitor (SNRI) and has been available since 1995. It is licensed for the treatment of depressive illness and generalised anxiety disorder (GAD).

The recommended dose for the treatment of depression is 75 to 150 mg a day.<sup>1</sup> It is also available as a modified release formulation; Efexor XL<sup>®</sup> (75 mg and 150 mg capsules) Severely depressed or hospitalised patients may need up to 375 mg daily. The recommended dose for GAD is 75 mg. Only Efexor XL<sup>®</sup> is licensed for the treatment of GAD.<sup>2</sup> Venlafaxine is not recommended for use in children and adolescents under 18 years old.<sup>1,2</sup>

### *Cardiotoxicity*

Venlafaxine increases the heart rate, particularly at high doses; the mean increase is 4 beats/min relative to baseline.<sup>1,3</sup>

Significant electrocardiogram findings were observed in 0.8% of venlafaxine-treated patients compared with 0.7% of placebo-treated patients.<sup>1,2</sup> In patients treated for depression it prolonged the QT interval (QTc) relative to placebo (increase of 4.7 msec for venlafaxine XL and a decrease of 1.9 msec for placebo).<sup>4</sup>

### *Toxicity in overdose*

Data from the General Register Office for Scotland and the Office for National Statistics for the years 1993-9 show that acute poisoning by venlafaxine, with or without co-ingestion of alcohol; is involved

in a higher rate of deaths from overdose than selective serotonin reuptake inhibitors (SSRIs).<sup>5</sup> The fatal toxicity index expressed as deaths per million prescriptions is higher for venlafaxine than those for other SSRIs and similar to those less toxic tricyclic antidepressants, e.g. trimipramine and clomipramine.<sup>5</sup> This may be explained by increased toxicity in overdose or use in patients at higher risk of suicide. Three further retrospective reviews of overdoses involving venlafaxine have been published involving 773 patients.<sup>6,7,8</sup> All recovered uneventfully although 45 (6%) developed convulsions.

### *CSM expert working group on the safety of SSRIs – a summary*

In December 2004 the CSM Expert Working Group published a report on the safety of SSRIs. While not an SSRI, venlafaxine was included in the review because it shares some of the properties of the SSRIs.<sup>9</sup> The CSM claim that venlafaxine may affect cardiac function. In addition, it may also be one of the drugs more likely to cause withdrawal reactions than some other SSRIs.<sup>9</sup>

### *When should it be used?*

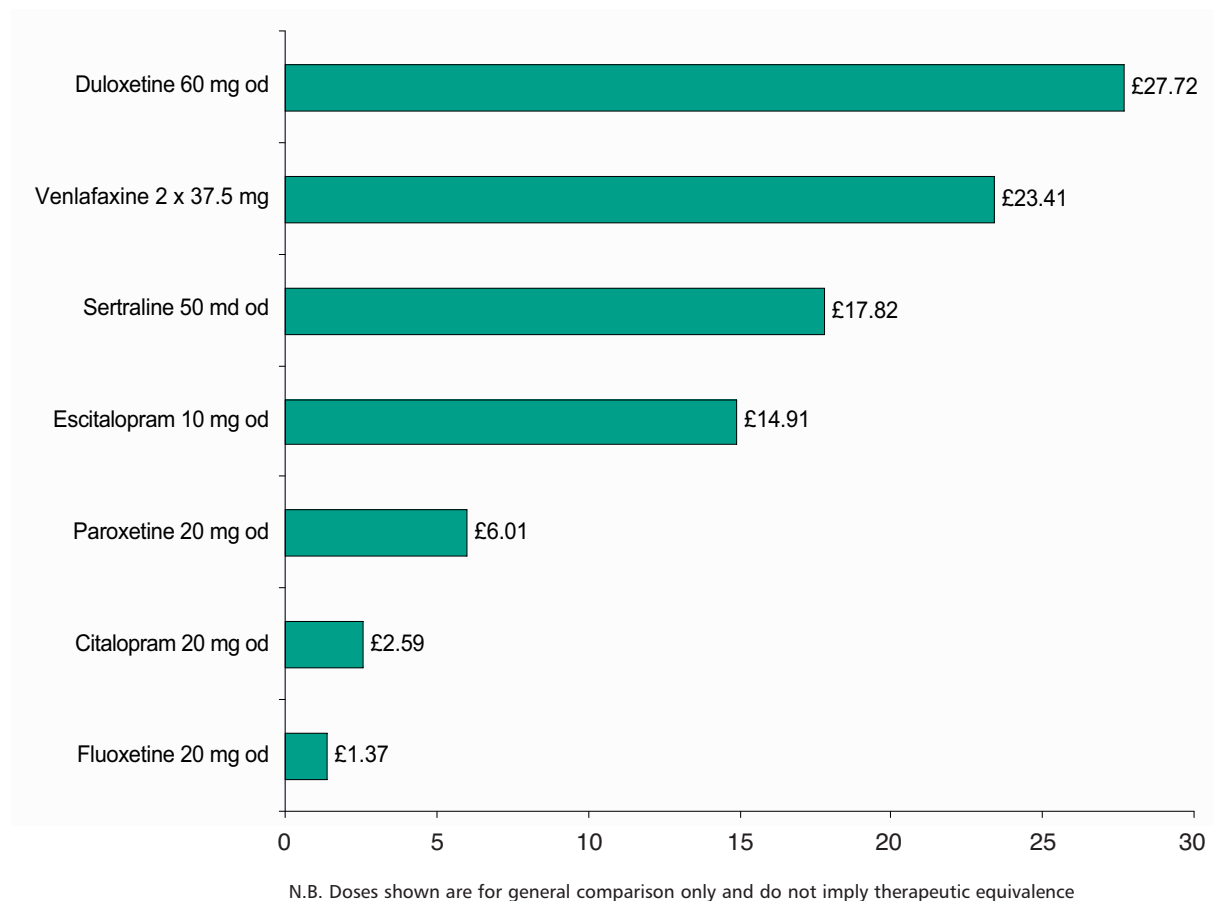
Guidelines issued in December 2004 by the National Institute for Clinical Excellence (NICE) for the management of people with depression and anxiety, recommend that venlafaxine should be considered only for patients whose depression has failed to respond to adequate trials of two other antidepressants and should not be prescribed for

patients with pre-existing heart disease.<sup>10</sup> It advised that patients taking venlafaxine are more likely to stop treatment due to side effects and withdrawal symptoms occur more commonly if stopped abruptly. Before starting treatment an ECG and blood pressure measurement should be undertaken. Consideration should be given to monitoring of cardiac function.<sup>10</sup> Regular monitoring of blood

pressure should be undertaken, particularly for those patients taking higher doses.<sup>10</sup> Regulatory action based on this advice is subject to an appeal. In the North of England the total number of prescriptions for venlafaxine rose by 78% from 2001/2 to 2004/5. A similar rise of 82% was seen in the Greater Manchester area over the same period.

### How much does it cost?

Approximate cost of 28 days treatment (Drug Tariff December 2005)



### REFERENCES

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- 8 Whyte IM et al. Relative toxicity of venlafaxine and selective serotonin reuptake inhibitors in overdose compared to tricyclic antidepressants. *Q J Med* 2003;96:369-74 (R)
- 9 Report of the CSM expert working group on the safety of selective serotonin reuptake inhibitor antidepressants [www.mhra.gov.uk](http://www.mhra.gov.uk) accessed 19.08.05 (G)
- 10 National Institute for Clinical Excellence. Depression. Management of depression in primary and secondary care. Clinical Guideline 23. December 2004 (G)

KEY G - guidelines, R-review, U-unpublished, A-abstract

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