



**Indian Health Service**  
**IHS National Pharmacy and Therapeutics Committee**  
**Formulary Brief:**  
**Serotonin-Norepinephrine Reuptake Inhibitors**  
**May 2012**



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**Background:**

The IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed the serotonin-norepinephrine reuptake inhibitors (SNRI) at the January and April 2012 meetings. They discussed their use in the management of depression and for their use as adjunct for the management of pain. Venlafaxine (long-acting) was **added** to the IHS National Core Formulary (NCF) and the NPTC recommended the development of a formulary brief for its use as an adjunct for pain management.

**Discussion:**

Venlafaxine is a SNRI agent that has FDA approved indications for use in generalized anxiety disorder, major depressive disorder, panic disorder and social phobia. It also has many off-label uses, including its use as an adjunct for pain management. It is available as a 37.5mg, 75mg and 150mg extended release capsule or 37.5mg 75mg, 150mg and 225mg extended release tablet. The extended release products are dosed once daily.

Pain is a common reason for patients to visit health care facilities. Pain and depression often coexist with studies reporting this combination in 30-60 percent of patients.<sup>1,2</sup> Neuropathic pain is found frequently in practice and often an associated complication of uncontrolled diabetes. Up to 25 percent of diabetic patients may develop neuropathic pain. Management options include tricyclic antidepressants, anticonvulsants, opioids, topical agents, SNRI's and combination therapy. Medications from these classes on the NCF include amitriptyline, imipramine, nortriptyline, divalproex and gabapentin.<sup>3</sup>

A 2007 systematic review from the Oregon Health and Sciences University Drug Effectiveness Review Project (DERP) assessed the various agents for use in neuropathic pain.<sup>4</sup> They found no head to head trials comparing the various agents against each other. An "adjusted indirect comparison of placebo controlled trials found gabapentin, duloxetine and venlafaxine similarly effective for pain relief and improvement in function compared to each other." Venlafaxine was compared to imipramine and found to be as effective as imipramine. Cochrane Reviews from 2007 and 2010 looked at antidepressant for neuropathic pain.<sup>5,6</sup> Their review calculated a number needed to treat (NNT) of 3.1 (95% CI 2.2 to 5.1) for patients treated with venlafaxine to achieve at least a moderate reduction in pain. Similar results were seen with tricyclic antidepressants (NNT 3.6; 95% CI 3 to 4.5). A 2004 study compared venlafaxine extended release to placebo and found a statistically significant reduction in pain intensity (placebo 27%, 75mg Ven=32%, 150-225mg=50%;  $p<0.001$ ) with a NNT of 4.5 to achieve a 50% reduction in pain.<sup>7</sup> The IHS Division of Diabetes Treatment and Prevention treatment algorithm lists TCA's as first line agents, followed by calcium channel modulators and SNRI's as second line.<sup>8</sup>

**Findings:**

Due to the frequent overlap of pain and depression, having agents from multiple drug classes is an important consideration. Venlafaxine has multiple indications for use in behavioral health. Venlafaxine also has good clinical data for its use as an adjunct for pain. Venlafaxine (long-acting) also has favorable pharmacoeconomic and utilization data across the IHS. The use of

products once daily versus multiple daily doses improves medication adherence. It was for these reasons, the IHS NPTC added Venlafaxine (long acting) to the IHS National Core Formulary.

If you have any questions regarding this document, please contact the NPTC at [nptc1@ihs.gov](mailto:nptc1@ihs.gov).

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