

Mergers and Acquisitions Among Psychotropics: Antidepressant Takeover of Anxiety May Now Be Complete

Stephen M. Stahl, M.D., Ph.D.

Issue: *Antidepressants are taking over the treatment of anxiety disorders. Essentially all forms of anxiety can now be treated with a variety of agents first introduced for the treatment of depression.*

Antidepressant or Anxiolytic?

Original drug classifications from the 1960s through the 1970s and into the 1980s emphasized that there were important distinctions between the antidepressants (e.g., tricyclic antidepressants) and the anxiolytics (e.g., benzodiazepines and buspirone) available at that time.¹ This emphasis reflected the diagnostic notions prevalent at that time, which tended to dichotomize major depressive disorder (MDD) from generalized anxiety disorder (GAD) while largely lumping all anxiety disorder subtypes together in the generalized anxiety disorder category. As time has progressed, there has been great interest in the middle ground between the entities of depression and anxiety, with essentially all antidepressants being recognized as effective in treating patients with MDD and symptoms of anxiety, and with anxiolytics being recognized as

effective in treating patients with GAD and symptoms of depression.^{1,2}

SSRIs as Psychotropic Raiders of the Anxiety Disorder Subtypes

The first hints of a breakdown in the distinction between an antidepressant and an anxiolytic came from indications in the 1970s and 1980s that certain tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors were effective in treating panic disorder and one TCA (clomipramine) was effective in treating obsessive-compulsive disorder (OCD).¹⁻³ This, in turn, accelerated the trend to more precisely subtype anxiety disorders and split them away from GAD. However, raiding of anxiety disorder subtypes by antidepressants did not come into full force until the 1990s as selective serotonin reuptake inhibitors (SSRIs) acquired their broadened efficacy profiles extending from depression first to OCD, then to panic disorder, now to social phobia, and perhaps soon to posttraumatic stress disorder (PTSD).¹⁻³ Benzodiazepines have fallen into the role of second-line treatments or augmentation treatments for these anxiety disorder subtypes in the 1990s. While buspirone continues to be recognized as a first-line general anxiolytic, it has not developed a convincing efficacy profile for these anxiety disorder subtypes.

Not all antidepressants, however, are successful raiders of the anxiolytic cupboard and thus have not taken over an anxiety claim. For example, desipramine and bupropion seem to be of very little help in treating anxiety disorder subtypes.³ Documentation of efficacy for several antidepressants other than SSRIs in treating anxiety disorder subtypes is preliminary at best, but some reports in individual cases and small trials have shown nefazodone, mirtazapine, and venlafaxine to be efficacious for various anxiety disorder subtypes, especially panic disorder and PTSD.³

When Is an Antidepressant an Antidepressant and When Is It a Generalized Anxiolytic?

Recently, venlafaxine XR became the first agent approved to treat both mood in depression and anxiety in GAD.^{4,5} Thus, the final gap in the great divide between antidepressants and anxiolytics has been bridged. Numerous agents have attempted in the past, but without success, to receive approval both as antidepressants and general anxiolytics. Early attempts to show that TCAs were also effective as general anxiolytics were promising but came after the TCA era was already over.⁶ TCAs appear to be slower in onset but perhaps more robust in efficacy even than benzodiazepines. In-

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From the Clinical Neuroscience Research Center in San Diego and the Department of Psychiatry at the University of California San Diego.

Reprint requests to: Stephen M. Stahl, M.D., Ph.D., Editor, BRAINSTORMS, 8899 University Center Lane, Suite 130, San Diego, CA 92122.

dividual reports and small trials have also shown mirtazapine, nefazodone, and paroxetine to be efficacious for GAD,⁷⁻⁹ but no approved antidepressant other than venlafaxine XR is widely recognized yet as effective for GAD.

Get the Patient All the Way Well— Do Not Just Convert Depression With Anxiety Into Anxiety Without Depression

Given the high degree of comorbidity of depression with generalized anxiety as well as anxiety disorder subtypes, the “holy grail” of a psychotropic has been to combine antidepressant with anxiolytic action in the same drug. Otherwise, patients treated with an antidepressant that is ineffective for their comorbid anxiety states will improve their symptoms of depression and continue to suffer from symptoms of anxiety. Alternatively, two agents must be given concomitantly, one effective for the depression and the other effective for the anxiety disorder.

In the SSRI era, prescribers are doing a better and better job of treating depression and anxiety disorder subtypes simultaneously, and often with only one drug. This is not always true, however, for patients with comorbid MDD and GAD. In such cases, depression is often targeted first in the hierarchy of symptoms, with the result that some patients may “respond” by decreasing their overall symptoms of depression, but continue to have generalized symptoms of anxiety rather than “remitting” completely to an asymptomatic state of “wellness.”¹⁰ Given the recent good news about venlafaxine XR and the promising trends of other antidepressants, it may now be possible, more than ever, to eliminate symptoms of both mood and

anxiety in the common situation where patients have both MDD and GAD and thus return them to a state of “wellness” with neither depression nor anxiety.¹⁰

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Take-Home Points

- ◆ For the first time, a drug, venlafaxine XR, originally approved as an antidepressant has also received dual approval as a general anxiolytic for generalized anxiety disorder.
- ◆ This brings full circle a trend started by the selective serotonin reuptake inhibitors fluoxetine, sertraline, paroxetine, fluvoxamine, and citalopram. These drugs were first recognized as approved treatments for depression but have now expanded their profiles as approved treatments for various anxiety disorder subtypes including obsessive-compulsive disorder, as well as panic disorder and, potentially, social phobia and posttraumatic stress disorder.
- ◆ This trend of antidepressants merging with anxiolytics and taking over the treatment of anxiety disorders looks to be expanding as many agents originally launched as antidepressants are showing promise for the treatment of a broad spectrum of anxiety disorders.