

## Venlafaxine discontinuation syndrome: Prevention and management

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### Disclosure

The author reports no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Most antidepressants lead to adverse discontinuation symptoms when they are abruptly stopped or rapidly tapered. Antidepressants with a short half-life, such as paroxetine and venlafaxine, can cause significantly more severe discontinuation symptoms compared with antidepressants with a longer half-life.

### One culprit in particular

Among serotonin-norepinephrine reuptake inhibitors (SNRIs), venlafaxine is notorious for severe discontinuation symptoms. Venlafaxine has a half-life of 3 to 7 hours, and its active metabolite, desvenlafaxine, possesses a half-life of 9 to 13 hours. Higher frequency of discontinuation symptoms is associated with the use of higher dosages of venlafaxine and longer duration of treatment.

Venlafaxine is available in immediate release (IR) and extended release (XR) formulations. Venlafaxine XR has a slower release, extending the time to peak plasma concentration and, therefore, has once daily dosing and fewer side effects; however, it offers no substantial advantage over IR formulation in terms of diminished withdrawal effects. Desvenlafaxine also is marketed as an antidepressant and, although one can speculate that the drug would have a lower rate of discontinuation symptoms than venlafaxine, no evidence supports this hypothesis.

A range of venlafaxine discontinuation symptoms have been reported (Table).<sup>1</sup>

### Preventing discontinuation symptoms

Patients for whom venlafaxine is prescribed should be informed about discontinuation symptoms, especially those who have a his-

tory of noncompliance. Monitor patients closely for discontinuation symptoms when venlafaxine is stopped—even if the patient is switched to another antidepressant. A gradual dosage reduction is recommended rather than abrupt termination or rapid dosage reduction. Immediately switching from venlafaxine to a selective serotonin reuptake inhibitor (SSRI) generally is not recommended, although it could alleviate some discontinuation symptoms<sup>2</sup>; cross-taper medication over 2 to 3 weeks.

Switching from venlafaxine to another SNRI, such as duloxetine, is less well studied. At venlafaxine dosages of <150 mg/d, an immediate switch to another SNRI of equivalent dosage generally is well-tolerated. For higher dosages, a gradual cross-taper is advised.<sup>2</sup>

Most patients tolerate a venlafaxine dosage reduction by 75 mg/d, at 1-week intervals. For patients who experience severe discontinuation symptoms with a minor dosage reduction, venlafaxine can be tapered over 10 months with approximately 1% dosage reduction every 3 days. Stahl<sup>3</sup> recommends dissolving the tablet in 100 mL of juice, discarding 1 mL, and



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**Table**

## Symptoms of venlafaxine discontinuation syndrome<sup>a</sup>

<b>Psychological</b>
Agitation
Anorexia
Anxiety
Confusion
Dysphoric mood
Hypomania
Insomnia
Nightmares
<b>Neurologic</b>
Dizziness and vertigo
Fasciculation
Fatigue, headache
Impaired coordination and balance
Paraesthesias and sensory disturbances
Somnolence
Tremor
<b>Physical</b>
Dry mouth
Flu-like symptoms
Nausea
Vomiting and diarrhea

<sup>a</sup>Not an exhaustive list  
**Source:** Reference 1

drinking the rest. After 3 days, 2 mL can be discarded, etc.

Another strategy to prevent discontinuation syndrome is to initiate fluoxetine—an SSRI with a long half-life—before taper; maintain fluoxetine dosage while venlafaxine is tapered; and then taper fluoxetine.

## Managing discontinuation symptoms

If your patient experiences significant discontinuation symptoms, resume the last prescribed venlafaxine dosage, with a plan for a more gradual taper. Acute discontinuation syndrome also can be treated by initiating fluoxetine, 10 to 20 mg/d; after symptoms resolve, fluoxetine can be tapered over 2 to 3 weeks.

### References

1. Effexor (venlafaxine hydrochloride) [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc; 2012.
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## Diagnosing and Managing Depressive Episodes in the DSM-5 Era

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### DISCUSSION INCLUDES:

- Applying the mixed features specifier
- Implications of mixed features for illness severity, comorbidities, and treatment response
- Management strategies

Diagnosing and Managing Depressive Episodes in the DSM-5 Era

CME Information  
 Release Date: October 1, 2015  
 Expiration Date: October 1, 2016  
 Estimated Time to Complete this Activity: 1 hour

**Overview**  
 This article provides a review of the particular challenges related to diagnosing bipolar and major depression disorders with mixed features and discusses the importance of accurate assessment of the mixed features specifier in order to provide optimal treatment for patients. Moreover, the differences between management of bipolar disorder with mixed features and major depressive disorder with mixed features will be addressed.

**Target Audience**  
 This activity has been designed to meet the educational needs of psychiatrists and mental health researchers who manage patients with depressive episodes.

**Educational Objectives**  
 After participating in this educational initiative, the participant should be better able to:

- integrate mechanisms for distinguishing unipolar and bipolar depression into the

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### Diagnosing and Managing Depressive Episodes in the DSM-5 Era

**The** premise of the newly introduced mixed features specifier in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* is similar to what was proposed approximately a century ago as part of the "manic-depressive" unification hypothesis. German psychiatrist Emil Kraepelin (1856-1926) originally conceptualized affective states as a continuum, wherein an individual's diagnosis was arrived at via a confluence of contemporaneous disturbances in mood, thought processes, and volition (behavior). His original description was agnostic insofar as it lacked the 2 categorical constructs, bipolar disorder and major depressive disorder—terms that eventually appeared in the DSM. Kraepelin described a total of 6 types of mixed states (depressive or anxious mania, excited depression, mania with thought poverty, manic stupor, depression with flight of ideas, and inhibited mania) and non-depression. The phenotypic variation of mixed states subsumed under the DSM-5<sup>1</sup>

**specifier** is specifier during a major depressive episode whose categorical diagnosis is a depressive disorder. The presence of triggering a major depressive episode in an order heuristically bridges bipolar disorder and is a tacit endorsement of an "The mixed features specifier in DSM-5 is of mixed states, which was defined as manic and depressive episode." The specifier is applied to an episode of hypomanic depressive features are present, as the DSM-5 or more proscribed by manic symptoms and juxtaposes the conceptual DSM-5. As can be seen in the figure, for a diagnosis of mania with mixed features, at least 3 core manic symptoms and at least 3 core depressive symptoms need to be present. For a diagnosis of depression with mixed features, at least 3 core manic symptoms and at least 5 depressive symptoms need to be present.<sup>2</sup>

Several core and nonoverlapping symptoms exist in depression with mixed features. Symptoms that are core (ie, allowed) include diminished interest or pleasure; slowed physical and emotional reac-

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