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).1

Preventing discontinuation symptoms
Patients for whom venlafaxine is prescribed should be informed about discontinuation symptoms, especially those who have a history 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; 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.2

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. Stahl3 recommends dissolving the tablet in 100 mL of juice, discarding 1 mL, and...
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

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*Not an exhaustive list

Source: Reference 1

Most patients tolerate a venlafaxine dosage reduction by 75 mg/d, at 1-week intervals

## Table
Symptoms of venlafaxine discontinuation syndrome

### Psychological
- Agitation
- Anorexia
- Anxiety
- Confusion
- Dysphoric mood
- Hypomania
- Insomnia
- Nightmares

### Neurologic
- Dizziness and vertigo
- Fasciculation
- Fatigue, headache
- Impaired coordination and balance
- Paraesthesias and sensory disturbances
- Somnolence
- Tremor

### Physical
- Dry mouth
- Flu-like symptoms
- Nausea
- Vomiting and diarrhea

*Not an exhaustive list

Source: Reference 1

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

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