

## How to reduce overdose risk with 'super benzodiazepine' atypicals

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Monitor for adverse respiratory events when prescribing atypicals alone or with any traditional CNS depressants

**A** new pattern of morbidity and mortality in suicidal patients who overdose has emerged with the broader use of atypical antipsychotics.<sup>1</sup> Although it is not known how often antipsychotics and benzodiazepines are combined in suicide attempts, clinicians need to prescribe atypicals carefully to prevent their use in self-poisoning.

We recently treated nonpsychotic patients whose most common clinical presentation after overdosing on some atypicals was near-fatal respiratory outcomes.

The FDA has warned of the risk of potentially fatal respiratory depression with concomitant administration of antipsychotics and benzodiazepines.<sup>2</sup> Each atypical carries a different respiratory warning and precaution. This observation prompted us to review the package inserts of the 3 "super benzodiazepine" atypicals.

**Clozapine** is a dibenzodiazepine. Its black-box warning states, "Since collapse, respiratory arrest, and cardiac arrest during initial treatment has occurred in patients who were being administered benzodiazepines or other psychotropic drugs, caution is advised when clozapine is initiated in patients taking a benzodiazepine or any other psychotropic drug."<sup>3</sup>

**Olanzapine** is a thienobenzodiazepine. Its precaution states, "co-administration of intramuscular lorazepam and intramuscular olanzapine for injection added to the somnolence observed with either drug alone. Concomitant administration of intramuscular olanzapine and parenteral benzodiazepine has not been studied and is therefore not recommended."<sup>3</sup>

**Quetiapine** is a dibenzothiazepine. Its precaution states, "The mean oral clearance

of lorazepam (2 mg, single dose) was reduced by 20% in the presence of quetiapine administered as 250 mg PO tid dosing."<sup>3</sup>

**Recommendations.** Because psychiatric patients have higher respiratory mortality than the general population, monitor patients' pulmonary status when administering these 3 atypicals as one might when prescribing benzodiazepines. Note:

- preexisting conditions that compromise respiratory function such as chronic obstructive pulmonary disease, sleep apnea, asthma, or pneumonia
- clinical indicators of changes in respiratory function, such as respiratory rate, dyspnea, hypoxemia, and acidosis.

Be cautious of adverse respiratory events when prescribing atypicals alone or with any traditional CNS depressants such as benzodiazepines, sedative/hypnotics, minor tranquilizers, sleep aids, opiates, methadone, and GABAminergic agents. Controlling the amount of antipsychotics dispensed could minimize the risk of overdose. Screen for depression before prescribing a combination of atypicals and CNS depressants. Consider prescribing other atypicals—not "super benzodiazepines"—to patients with possible suicide risk.

### References

1. Viner MW, Chen Y, Bakshi I, et al. Low-dose risperidone augmentation of antidepressants in nonpsychotic depressive disorders with suicidal ideation. *J Clin Psychopharmacol* 2003;23:105-6.
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3. *Physicians' desk reference*. 62nd ed. Montvale, NJ: Thomson Healthcare Inc.; 2007.

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