

# Letter to the Editor

## Uses of Newer Anticonvulsants: An Update

**Sir:** Since the publication of a recent review of the psychiatric uses of newer anticonvulsants in the *Companion*,<sup>1</sup> 2 new anticonvulsants have come to market. The first is levetiracetam, which is U.S. Food and Drug Administration–approved as an adjunctive agent in treating partial-onset seizures in adults with epilepsy.<sup>2</sup> Its precise mechanism of action is not known, but does not appear to be due to any interaction with known mechanisms involved in inhibitory or excitatory neurotransmission.<sup>3</sup> Levetiracetam possesses a unique pharmacologic profile, a high margin of safety, and potential antiepileptogenic properties by potent inhibition of kindling.<sup>4</sup> The principal route of elimination is renal, with about 66% of a dose excreted unchanged.<sup>5</sup> To date, there are no published data on levetiracetam and bipolar disorder. However, 2 pilot studies on the treatment of bipolar disorder with levetiracetam are ongoing.<sup>6,7</sup> There is 1 case report on the use of levetiracetam as monotherapy in acute mania in a patient who had failed more conventional mood stabilizers.<sup>8</sup>

The second new agent is zonisamide, approved as an add-on agent for partial seizures in adults.<sup>9</sup> It appears to have several mechanisms of action, including blockade of voltage-sensitive sodium channels and T-type calcium currents, modulation of dopaminergic and GABAergic systems, and free-radical scavengers.<sup>10</sup> The drug, which has been used in Japan for over 11 years as an anticonvulsant, is metabolized through the liver, is a mild liver enzyme inducer, and is titrated slowly.<sup>11</sup> Because zonisamide has been used in Japan since 1989,<sup>10</sup> most of the published data describing psychiatric uses are in Japanese without translation.<sup>12–14</sup> To date, there is 1 open-label add-on study in English examining zonisamide as an adjunct in 24 patients with mania (15 diagnosed with bipolar mania; 6, with schizoaffective manic state; and 3, with schizophrenic excitement).<sup>15</sup> Eighty percent of the bipolar patients, 66% of the schizoaffective patients, and 50% of the schizophrenic patients showed a moderate to remarkable improvement by the end of the fourth or fifth week.<sup>15</sup> Kanba and Yagi<sup>16</sup> earlier studied zonisamide in 6 patients with acute mania; 2 patients responded very well to zonisamide monotherapy, 1 patient with rapid cycling experienced a decrease in the severity of the episode, 1 schizoaffective patient stabilized, 1 schizoaffective patient progressed from hypomania to moderate depression, and 1 patient with mania did not respond to treatment. More data obtained in a controlled fashion will be required to determine if these new agents will prove to be of value in treating psychiatric disorders.

*Dr. Berigan reports no financial affiliation or other relationship relevant to the subject matter of this letter.*

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