Mr. B, age 64, is being treated in the psychiatric clinic for generalized anxiety disorder. He also has a history of type 2 diabetes mellitus and osteoarthritis. His present medications include metformin 500 mg twice daily, escitalopram 20 mg/d, and a multivitamin.

Three months after a shingles outbreak on his left trunk, Mr. B develops a sharp, burning pain and hypersensitivity to light in the same area as the shingles flare-up. He is diagnosed with postherpetic neuralgia. Despite a 12-week trial of cognitive-behavioral therapy, Mr. B continues to report excessive worry, irritability, poor concentration, psychomotor restlessness, and poor sleep.

Contrasting with the serendipitous discovery of iproniazid and chlorpromazine leading to the development of the current spectrum of antidepressant and antipsychotic agents, discovery of the benefits various antiepileptic agents have in bipolar disorder has not led to a similar proliferation of medication development for bipolar mania or depression.1-3 Divalproex, one of the most commonly used antiepileptic drugs (AEDs) in psychiatry, was thought to be an inactive organic solvent until it was used in 1962 to test the anticonvulsant activity of other compounds. This led to the discovery and subsequent use of divalproex in patients with epilepsy, followed by FDA approval in bipolar disorder.4,5 Off-label use of many AEDs as mood-stabilizing agents in bipolar disorder led to the emergence of carbamazepine, divalproex, and lamotrigine, which joined lithium as classic mood-stabilizing agents.6-8 Amid varying definitions of “mood stabilizer,” many AEDs have failed to demonstrate mood-stabilizing effects in bipolar disorder and therefore should not all be considered mood stabilizers.9 Nonetheless, the dual use of a single AED for both psychiatric and nonpsychiatric indications can decrease polypharmacy and increase acceptability of medications in patients who have low insight into their illness.10,11

Practice Points

• The use of individual antiepileptic drugs (AEDs) for dual indications—psychiatric and nonpsychiatric—can decrease polypharmacy and increase acceptability of medications in situations where patient insight into their illness may be low.

• Dual use of AEDs for psychiatric and nonpsychiatric indications requires appreciation and consideration of indication-specific dosing.

• Limitations, such as drug-drug interactions and the propensity for AEDs to cause suicidality, should be considered when prescribing AEDs for both psychiatric and nonpsychiatric indications.
### Table

#### Mood stabilizers and select antiepileptics with common psychiatric and nonpsychiatric indications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Psychiatric indication(s)</th>
<th>Nonpsychiatric indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carbamazepine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Off-label: Bipolar depression[^9,17] maintenance treatment for bipolar disorder[^10,18,19]</td>
<td></td>
</tr>
<tr>
<td><strong>Divalproex</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MDD: major depressive disorder; RLS: restless leg syndrome

[^...]: References omitted for brevity.
Because AEDs were originally purposed to treat neurologic disease, psychiatric indications must first be established before considering other indications. AEDs as a class have broad pharmacologic actions, but are generally CNS depressants, decreasing brain signaling through mechanisms such as ion channel antagonism (carbamazepine, gabapentin) or alterations to gamma-aminobutyric acid/glutamate signaling (divalproex, topiramate).

Compared to antidepressants and antipsychotics, whose primary use for psychiatric conditions is firmly rooted in evidence, rational use of AEDs for psychiatric conditions and symptoms depends on the agent-specific efficacy. Patients with comorbid psychiatric and neurologic disorders are ideal candidates for dually indicated AEDs due to these agents’ class effects rooted in epilepsy. Due to the history of positive psychiatric benefits with AEDs, newer agents may be psychiatrically beneficial but will likely follow the discovery of these benefits in patients for whom epilepsy is the primary diagnosis.

Consider the limitations

Using AEDs to reduce polypharmacy should be done judiciously from a drug-drug interaction perspective, because certain AEDs (eg, carbamazepine, divalproex) can greatly influence the metabolism of other medications, which may defeat the best intentions of the original intervention.

Several other limitations should be considered. This article does not include all AEDs, only those commonly used for psychiatric indications with known nonpsychiatric benefits. Some may worsen psychiatric conditions (such as rage and irritability in the case of levetiracetam), and all AEDs have an FDA warning regarding suicidal behaviors and ideation. Another important limitation is the potential for differential dosing across indications; tolerability concerns may limit adequate dosing across multiple uses. For example, topiramate’s migraine prophylaxis effect can be achieved at much lower doses than the patient-specific efficacy dosing seen in binge eating disorder, with higher doses increasing the propensity for adverse effects.

Dual-use AEDs should be considered wherever possible, but judicious review of evidence is necessary to appropriately adjudicate a specific patient’s risk vs benefit. The Table provides information on select AEDs with both psychiatric and nonpsychiatric indications, including both FDA-approved and common off-label uses. These indications are limited to adult use only.

CASE CONTINUED

After reviewing Mr. B’s medical history, the treating medical team decides to cross-taper escitalopram to duloxetine 30 mg twice daily. Though his pain lessens after several weeks, it persists enough to interfere with Mr. B’s daily life. In addition to duloxetine, he is started on pregabalin 50 mg 3 times a day. Mr. B’s pain decreases to a tolerable level, and he reports decreased worrying and restlessness, and improvements in concentration and sleep.

References
Keep in mind that certain AEDs (eg, carbamazepine, divalproex) can greatly influence the metabolism of other medications.

**Clinical Point**

Tolerability concerns may limit adequate dosing across multiple uses.