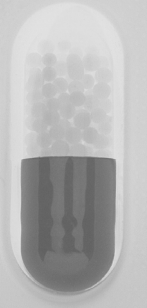


Mood Stabilizers



Anticonvulsants

Carbatrol, Tegretol, and Tegretol-XR (carbamazepine)

Depakene (valproic acid) and Depakote (divalproex)

Lamictal (lamotrigine)

Neurontin (gabapentin)

Topamax (topiramate)

Trileptal (oxcarbazepine)

Lithium Carbonate and Lithium Citrate

Eskalith

Eskalith-CR

Lithium Citrate

Lithobid

Lithotab

Second-Generation Antipsychotics

Abilify (aripiprazole)

Clozaril (clozapine)

Geodon (ziprasidone)

Risperdal (risperidone)

Seroquel (quetiapine)

Zyprexa (olanzapine)

Simply defined, mood stabilizers are medicines used in treating mood disorders such as bipolar disorder and depression. Bipolar disorder is characterized by mood swings in which the individual cycles between mania and depression. The symptoms fluctuate from euphoria and limitless energy in the manic phase to the depths of depression with little energy, guilt, sadness, decreased concentration, lack of appetite, and sleep disturbance. Because of the wide range of symptoms, from mania to depression, bipolar disorder is often called **manic depression**.

Mood stabilizers are used to treat **acute mania**, **hypomania** (a mild form of mania), mixed episodes (when mania and depression coexist in an episode), and **depression**. Following the acute episode, mood stabilizers are used in maintenance therapy to prevent the cyclical relapse of abnormal mood elevations and depressions.

The goals of maintenance treatment with a mood stabilizer are to 1) reduce residual symptoms, 2) prevent manic or depressive relapse, 3) reduce the frequency of cycling into the next manic or depressive episode, 4) improve functioning, and 5) reduce the risk of suicide.

Lithium

Lithium was one of the first mood stabilizers used in the treatment of bipolar disorder. Lithium is a simple ion not unlike sodium found in table salt (sodium chloride). Lithium comes in two forms—lithium carbonate and lithium citrate. Lithium carbonate is available in immediate- and controlled-release capsules and tablets. Lithium also comes in a liquid preparation in the form of lithium citrate. Over several decades of clinical experience, lithium has been shown to be effective not only in treating mania but also in preventing relapse of mania and depression in bipolar disorder. Lithium was the most important mood stabilizer for many years, but another mood stabilizer—Depakote (divalproex)—has since surpassed lithium for the treatment of bipolar disorder. The reason is that lithium has many troublesome side effects, including nausea, diarrhea, weight gain, and mental sluggishness, and there is a risk of lithium toxicity when the amount of lithium, as measured by serum levels, exceeds its narrow therapeutic range. Monitoring of lithium blood levels is very important to prevent lithium toxicity. (For further information, refer to the handout on “Lithium.”)

Anticonvulsants as Mood Stabilizers

The introduction of anticonvulsants to the treatment of mood disorders emerged as one of the most significant advances in modern psychiatry. Tegretol (carbamazepine) has been used for more than two decades to treat bipolar disorder without an approved indication for this purpose from the U.S. Food and Drug Administration (FDA). Depakote (divalproex) and Lamictal (lamotrigine) are the only two anticonvulsants approved by the FDA for treatment of seizure and bipolar disorders; the other anticonvulsants are indicated primarily for treatment of epilepsy. The use of a medication for its approved indication is called *labeled use*. In clinical practice, however, physicians often prescribe medications for *unlabeled* (“off-label”) uses when published clinical studies, case reports, or their own clinical experiences support the efficacy and safety of those treatments. Based on a number of clinical studies, some medications with anti-epileptic properties are also effective for treating bipolar disorder, despite the lack of an FDA-approved indication for this purpose.

Some may wonder why an anticonvulsant that is effective for controlling seizures also works for bipolar disorder. How is this paradox explained? The application of anticonvulsants in psychiatry was due in part to serendipity. With certain types of epilepsy, individuals sometimes manifest psychiatric symptoms, including hallucinations, agitation, and changes in mood. When such patients were treated with phenytoin (Dilantin), an anticonvulsant, their seizures, as well as their psychiatric symptoms, were stabilized. These observations spurred clinical investigations of other anticonvulsants, including carbamazepine and valproic acid (and valproate), to determine if they also offered benefits in treating mood disorders. A number of clinical studies have shown that Tegretol (carbamazepine), Depakote (divalproex sodium), and Lamictal (lamotrigine) are effective for bipolar disorder.

It is not totally clear why some anticonvulsants are effective for seizures and bipolar disorder. The anticonvulsants, which have very complex effects on the central nervous system, may be effective by controlling “kindling” in the areas of the brain from which the psychiatric disorder emanates. Kindling is a phenomenon that occurs when repeated subthreshold stimulation is applied to certain regions of the brain and sensitizes them, setting off a cascade of events leading to seizures or manic behavior. By decreasing electrical conduction or neurotransmitter activity in unstable brain cells, anticonvulsants are effective in controlling seizures and bipolar illness.

Second-Generation Antipsychotics as Mood Stabilizers

Antipsychotics are frequently prescribed in combination with a mood stabilizer, such as lithium or Depakote, to treat acute mania. An antipsychotic is helpful for rapidly reducing mania, especially during the interval of time until the mood stabilizer, which has a slower onset of action, takes effect. Generally, the psychiatrist would discontinue the antipsychotic after mania abates, maintaining mood stabilization with the mood stabilizer alone. This was the conventional practice when only the older, first-generation antipsychotics (e.g., Thorazine, Mellaril, Haldol, and Prolixin), were available. The long-term use of conventional antipsychotics was not advisable then because the older agents were associated with significant risks of **tardive dyskinesia** (disabling, late-onset movement disorders) and **extrapyramidal symptoms**, which are side effects that affect coordination and movement. Moreover, the conventional agents can exacerbate depressive symptoms in some patients. (Also, refer to the handout on “First-Generation Antipsychotics.”)

This strategy—that is, the long-term use of an antipsychotic to treat bipolar disorder—changed when the newer, second-generation antipsychotics became available. These antipsychotics have significantly reduced the risk of tardive dyskinesia and extrapyramidal symptoms and have fewer of the bothersome side effects commonly seen with the conventional agents. Furthermore, they appear to have a wider spectrum of therapeutic activity than the conventional agents. They can do more than just reduce mania; they appear to have mood stabilizing properties and can prevent relapse when used in maintenance therapy. Zyprexa (olanzapine), for example, is currently the only second-generation antipsychotic approved by the FDA for acute mania and maintenance therapy for relapse prevention in bipolar illness. The others are also effective anti-manic agents, but it is not clear whether they also possess mood-stabilizing properties for long-term maintenance therapy. However, some preliminary data show that other second-generation antipsychotics may be effective mood stabilizers as well. (Handouts for these antipsychotics can be found in “Second-Generation Antipsychotics.”)