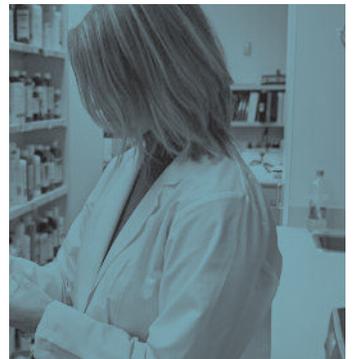


BEST BUY DRUGS™

Using Anticonvulsants to Treat

Bipolar Disorder, Nerve Pain, and Fibromyalgia:

Comparing Effectiveness, Safety, and Price



Our Recommendations

Anticonvulsant drugs are prescribed to treat a range of medical conditions in addition to seizure disorders, like epilepsy. Among those are bipolar disorder, fibromyalgia, and pain caused by nerve injuries (neuralgia) or other disorders.

Overall, study results showing how well anticonvulsants work in treating those three conditions are mixed, and varies by both specific drug and disorder. Other treatment options might work as well as or better than anticonvulsants. That said, some anticonvulsants have been linked to clear clinical benefits, and several have been approved by the Food and Drug Administration for treating bipolar disorder, nerve pain, or fibromyalgia.

Anticonvulsants can cause serious side effects, including an increased risk of suicide and life-threatening skin rashes. They can also cause dangerous interactions with other medications. Newer anticonvulsants marketed since the late 1990s have sometimes been touted as safer and posing less risk of adverse effects than older ones. No large, good quality studies have tested this directly, but small, short-term studies that compared the drugs don't support such a conclusion.

Taking cost, dosing convenience, effectiveness, safety, and adverse effects into consideration, we have chosen the following as *Consumer Reports Health Best Buy Drugs* if you and your doctor decide that an anticonvulsant might be appropriate:

- *Generic carbamazepine* – for treating the manic phases of bipolar disorder and for trigeminal neuralgia, a type of nerve pain that affects facial trigeminal nerves.
- *Generic valproic acid* or *generic divalproex* – for treating the manic phases of bipolar disorder.
- *Generic lamotrigine* – for treating the depressive phases of bipolar disorder.
- *Generic gabapentin* – for treating nerve pain associated with diabetes or herpes zoster infection (shingles), and for treating fibromyalgia.

This report was published in July 2011.

Welcome

This report evaluates a class of medications known as anticonvulsants or antiepileptic drugs. They are named as such because all are approved primarily to treat people who have various kinds of seizure disorders, including seizures or convulsions caused by epilepsy, strokes, or brain tumors.

Drugs in this class are also commonly prescribed to treat three other conditions: bipolar disorder, certain types of nerve pain, and a condition called fibromyalgia. In this report, we focus only on the use of anticonvulsants to treat those conditions. We do not evaluate the drugs to treat seizures or epilepsy.

Some anticonvulsants have been around for decades. Phenytoin (Dilantin) was approved in the U.S. in 1946, followed by carbamazepine (Carbatrol, Tegretol), and valproic acid (Depakene) or divalproex (Depakote). Together, these drugs and some of their off-shoots are often referred to as the “first generation” or older anticonvulsants.

A group of “second-generation” anticonvulsants was developed in the 1990s. Doctors use them along with the older ones to treat conditions other than seizures, including bipolar disorder and pain due to nervous-system damage, trauma, or dysfunction, also called nerve pain.

Nerve pain is different from other types of pain, like headaches or muscle and joint pain. Doctors also refer to it as neuropathic pain, or neuralgia. The typical symptoms include constant or intermittent tingling, burning, or numbness. Nerve pain can be caused by an injury or accident but often occurs in people with certain conditions, such as diabetes, which can lead to nerve damage. Shingles, caused by the chickenpox or herpes zoster virus, can also cause nerve pain. Sometimes the source of nerve pain is unknown. (See the box on page 7 for a more complete explanation.)

Fibromyalgia is a syndrome involving such symptoms as muscle pain, joint tenderness, fatigue, sleep disturbance, and a chronic low-grade, flu-like feeling. It’s often associated with chronic fatigue syndrome. Fibromyalgia can be mild, moderate, or severe. The diagnosis is controversial because there’s no definitive diagnostic test for it. (See the box on page 8 for a fuller explanation.)

The anticonvulsants we evaluate and compare in this report are:

The Older Anticonvulsants			
Generic Name	Brand Name	Available as a Generic?	Common Uses
Carbamazepine	Tegretol, Eptol, Carbatrol, Equetro, Tegretol-XR	Yes	Approved: <ul style="list-style-type: none"> ■ Manic phases in bipolar disorder ■ Facial nerve pain
Phenytoin	Dilantin, Phenytek	Yes	
Divalproex, Valproic acid	Depakene, Depakote, Depakote ER	Yes	Approved: <ul style="list-style-type: none"> ■ Manic phases in bipolar disorder Off-label: <ul style="list-style-type: none"> ■ Depressive phases in bipolar disorder ■ Nerve pain due to diabetes or shingles
The Newer Anticonvulsants			
Generic Name	Brand Name	Available as a Generic?	Common Uses
Gabapentin	Neurontin	Yes	Approved: <ul style="list-style-type: none"> ■ Nerve pain related to the shingles virus Off-label: <ul style="list-style-type: none"> ■ Nerve pain due to diabetes ■ Other chronic nerve pain ■ Fibromyalgia
Lacosamide	Vimpat	No	
Lamotrigine	Lamictal	Yes	Approved: <ul style="list-style-type: none"> ■ Manic phases in bipolar disorder Off-label: <ul style="list-style-type: none"> ■ Depressive phases in bipolar disorder ■ Chronic nerve pain
Levetiracetam	Keppra	Yes	
Oxcarbazepine	Trileptal	Yes	Off-label: <ul style="list-style-type: none"> ■ Manic phases in bipolar disorder ■ Nerve pain due to diabetes or shingles ■ Facial nerve pain

The Newer Anticonvulsants (continued)

Generic Name	Brand Name	Available as a Generic?	Common Uses
Pregabalin	Lyrica	No	Approved: <ul style="list-style-type: none"> ■ Nerve pain due to diabetes ■ Nerve pain related to the shingles virus ■ Fibromyalgia
Tiagabine	Gabitril	No	
Topiramate	Topamax	Yes	Off-label: <ul style="list-style-type: none"> ■ Nerve pain due to diabetes or shingles
Zonisamide	Zonegran	Yes	

The Food and Drug Administration (FDA) has approved certain anticonvulsants to treat bipolar disorder, certain types of nerve pain, and fibromyalgia. Specifically, divalproex, lamotrigine, and carbamazepine have been approved to treat the manic phases of bipolar disorder; carbamazepine, gabapentin (Neurontin), and pregabalin (Lyrica) have been approved to treat various forms of nerve pain; and pregabalin (Lyrica) has also been approved to treat fibromyalgia.

But many of the other anticonvulsants are also widely prescribed “off-label” (without FDA approval) to treat those conditions. While many drugs are prescribed effectively—and legally—off-label, we advise using caution with such prescriptions. Some of the old and new anticonvulsants are included on lists of drugs that are being too widely prescribed off-label without scientific support. Some have also been abused and misused by people who don’t have a legitimate medical need for them but obtain them illegally.

Importantly, anticonvulsants are only one of many treatment options for bipolar disorder, nerve pain, and fibromyalgia. For example, treatments for bipolar disorder include lithium, antipsychotic drugs, and professional counseling. Nerve pain and fibromyalgia are both commonly treated with antidepressant drugs and various other therapies, including transcutaneous electrical nerve stimulation (TENS), physical therapy, occupational therapy, biofeedback, exercise, relaxation therapy, meditation, and hypnosis.

It’s common for people with bipolar disorder, nerve pain, or fibromyalgia to try several medications or combinations of medications and non-drug treatments before finding adequate relief.

In terms of pricing, certain generic anticonvulsant medications cost as little as \$4 for a month’s supply through drug programs at Kroger, Sam’s Club, Target, Walmart, and other chain stores. Some drug programs offer even better bargains: a three-month supply for \$10. We note in the price chart starting on page 18 which generic medications are available through these programs. Some stores, such as CVS and Walgreens, require a membership fee to participate and might charge higher prices. There might be other restrictions too, so check the details carefully to make sure your drug and dose are covered.

This report is based on a comprehensive analysis of the medical evidence. From more than 2,500 studies that were screened, the analysis focused on 174 studies that directly compared one anticonvulsant drug to another or to other commonly used medicines or a placebo.

This report is part of a *Consumer Reports* project to help you find safe, effective medications that give you the most value for your health-care dollar. To learn more about the project and other drugs we’ve evaluated, go to ConsumerReportsHealth.org/BestBuyDrugs.

This report was published in July 2011.

What Are Anticonvulsants and Who Needs Them?

It's not clear how anticonvulsants reduce symptoms and maintain balance in people with bipolar disorder or relieve pain due to nerve damage or fibromyalgia. It's thought that they work by altering levels of chemicals in the brain and nervous system called neurotransmitters, and by reducing or blocking electrical signals in nerve and brain cells.

But all anticonvulsants don't work the same way. Each drug induces these changes in the brain and nervous system in a different way and affects individuals differently. A person might respond poorly to one anticonvulsant but quite well to another, for example.

Overall, the evidence for the effectiveness of anticonvulsants in treating people with bipolar disorder, nerve pain, or fibromyalgia is mixed. That said, some anticonvulsants have been linked to clear benefits for people with those conditions.

Study findings are mixed in part because of the nature of the three conditions. It's more difficult to gauge the success of drugs used to treat conditions that have a broad range of symptoms that are often subjective. Determining the effectiveness of treatments for bipolar disorder, nerve pain, and fibromyalgia depends, in large part, on a patient's own assessment of the relief he or she gets from a drug.

Your need for an anticonvulsant might not be clear-cut. Unlike the vast majority of people who take drugs for, say, high blood pressure, diabetes, or high cholesterol and will experience benefits that can be measured objectively by simple tests—some people who take an anticonvulsant might see an improvement while others get little or no benefit.

Also, as discussed above, other drugs and treatments exist for all three conditions. In some cases,

What Is Bipolar Disorder?

Everyone has times when they feel "up" and times when they feel "down." For some people, though, mood swings can be extreme, last much longer than normal, and occur for no apparent reason. Those people might have bipolar disorder, which affects about 5.7 million adult Americans, according to the National Institute of Mental Health.

Bipolar disorder has two distinct phases: mania and depression. In most cases, either mood can last for several weeks, and there is often an in-between period when people are in a "normal" or stable mood. About one-third to half of the people with bipolar disorder have a more severe form of it, with several episodes a year. The rest are less severely affected and may have months of stable mood between bouts of mania and depression.

Most people with bipolar disorder are more prone to shorter periods of mania (from a week to several weeks) and longer periods of depression (from several weeks to months).

Common symptoms of manic episodes:

- Feelings of extreme happiness and well-being
- Increased talkativeness
- Racing thoughts and ideas
- Reduced need for sleep
- Irritability
- Increase in risky behaviors (e.g., abuse of drugs or alcohol, spending sprees, sex with many partners)
- Increased impulsiveness

Common symptoms of depressive episodes:

- Feelings of unhappiness and despair
- Loss of interest or pleasure in previously enjoyed activities
- Decreased energy, extreme fatigue
- Trouble falling asleep, staying asleep, and/or early-morning awakening
- Difficulty concentrating
- Irritability/restlessness
- Increase or decrease in appetite
- Suicidal thoughts/attempts

those should be the initial or primary therapy. That's usually the case for most people with bipolar disorder, for example, for whom lithium is often a better choice than an anticonvulsant.

The need for anticonvulsants in treating nerve pain is more widely accepted and complex. Three medications—carbamazepine, gabapentin, and pregabalin—have been approved to treat nerve pain, although not all are approved for the same types of nerve pain. Other drugs and therapies are available that could be better for some patients. In addition, the long-term effectiveness and safety of anticonvulsants in treating nerve pain have not been studied extensively.

If you have been diagnosed with fibromyalgia, your need for an anticonvulsant is still unclear despite the recent approval of pregabalin (Lyrica) to treat the condition. Numerous studies show a type of antidepressant called a tricyclic benefits many people with fibromyalgia. Also, another type of antidepressant, duloxetine (Cymbalta), and one other drug, milnacipran (Savella), are approved by the FDA for treating the condition. We further discuss Lyrica's use to treat fibromyalgia in the next section.

What is Nerve Pain?

There are more than 100 types of nerve pain. It can occur in people with diabetes, alcoholism, kidney disease, cancer and human immunodeficiency virus (HIV), as well as from herniated discs, shingles (herpes zoster virus, which also causes chickenpox), the "phantom" pain of amputated limbs, or multiple sclerosis. Nerve pain can also occur following stroke, spinal cord injury, surgery, or other trauma to the body.

Nerve pain is often a chronic condition. For some, the pain may be constant, but for most people the symptoms come and go. It's usually burning, shooting, or piercing pain; an icy cold or intensely hot feeling; tingling or crawling; numbness; a pins-and-needles feeling; or intense itching.

The sensations can be mild to severe. Some of the more common conditions that cause nerve pain are:

- Diabetic neuropathy—a common complication of diabetes. About half of the 24 million people with diabetes in the U.S. will suffer from neuropathy at some point, and the incidence increases over time. About 20 percent of the people with diabetic neuropathy have nerve pain to varying degrees.
- Trigeminal neuralgia—involves the onset (usually sudden) of intense pain on one side of the face. The main sensory nerve in the area is called the trigeminal nerve.
- Postherpetic neuralgia—caused by nerve inflammation that occurs during and after an attack of shingles, which in turn is caused by the same virus that causes chicken pox (herpes zoster). As many as 1 million people in the U.S. suffer from this form of nerve pain at some point.
- Cancer-associated neuralgia—can be a direct result of the cancer impinging on nerves or cancer in a part of the nervous system itself. Also, certain kinds of chemotherapy can damage nerve cells and cause neuropathy.
- Compression neuropathy—occurs when a nerve is pressed by a slipped disc (sciatica) or by a ligament (carpal tunnel syndrome, for example).

What Is Fibromyalgia?

People with fibromyalgia can have a variety of symptoms, including muscle pain or soreness, joint tenderness or pain, tenderness to the touch, fatigue, sleep disturbance, and a chronic flu-like feeling. In addition, people diagnosed with fibromyalgia are more likely to have depression, anxiety, rheumatoid arthritis, lupus, Lyme disease, and chronic fatigue syndrome.

The cause is unknown, although it has been linked (inconclusively) to viral infections, exposure to toxins, and physical or emotional trauma. Some research suggests that it may stem from abnormal pain processing in the brain and spinal cord. That can result in a lowered threshold for pain and a heightened response to sensations that wouldn't be painful for healthy people.

About 5 million adults in the U.S. have fibromyalgia, according to the National Institute of Arthritis and Musculoskeletal and Skin Diseases. For reasons that are unclear, 80 to 90 percent of them are women. But the diagnosis is controversial. Many insurers are skeptical of the condition and reluctant to reimburse expenses incurred in treating it.

As with nerve pain, fibromyalgia symptoms vary in severity. Some people seem to have very mild symptoms while others have more severe and debilitating ones.

Studies indicate that fibromyalgia doesn't seem to worsen over time, but the symptoms can continue for years. For that reason, it's considered a chronic condition. But some people with fibromyalgia do seem to recover and cease having symptoms.

People with symptoms of fibromyalgia often consult many doctors. If you suspect you may have fibromyalgia, the important thing is to find a doctor who is familiar with the condition and can do a thorough evaluation to either confirm the diagnosis or rule it out.

Choosing an Anticonvulsant — Our *Best Buy* Picks

If you and your doctor decide to try an anticonvulsant, this section will help you consider your options and find one that might be the most appropriate for your situation. Each of the three conditions is discussed below.

One overriding issue with anticonvulsant drugs is whether the newer ones are better than the older ones. There is no consistent, clear evidence to support the newer anticonvulsants over the older ones. Indeed, there are no large, well-done studies that directly compare the effectiveness and safety of the older anticonvulsants to the newer ones for treating bipolar disorder, nerve pain, or fibromyalgia. But there are many that compare them in seizure disorders.

The older drugs have the advantage of having been prescribed for many years, so many doctors know their strengths, weaknesses, and risks quite well—and perhaps better—than the newer drugs. But older drugs have often not been studied in an adequate number of patients in good quality trials. That could be because these drugs are available as generics and their makers don't have an incentive to support extensive clinical trials. In addition, the older drugs can also require frequent dosing—three to four times a day—to be effective.

The newer drugs have their own set of problems and side effects. One possible advantage is that they generally require less-frequent dosing, although you might still need to take a pill two or more times a day.

One big difference between the older and newer drugs is cost. In general, the newer drugs are more expensive, but all of them except Gabitril, Lyrica, and Vimpat are now available as generics that will likely become less expensive over time. (See Table 3 on page 18.)

In choosing our *Best Buys*, we take into account effectiveness, side effects, safety, and costs. In addition, we consider dosing convenience. With these medicines in particular, your doctor might think that dosing convenience is very important

and choose a more expensive medicine on that basis. You might want to discuss the cost of the medicine with him or her if it's an important issue for you, for example, if you're uninsured or your co-payment for one anticonvulsant will be higher than for another.

Note also that the dosing regimens for anticonvulsant drugs usually involve taking a low dose initially followed by a steady increase in dose to achieve maximum benefit. Your doctor and pharmacist will give you instructions on when and how often to increase the dose.

As the dose is increased, it's important to talk with your doctor about whether you feel the drug is helping or not. With pain relief, that's easy to know. If it's not working, taking a low dose of an anticonvulsant for an extended period is a waste of money and time, since another drug might work better for you. So once you've reached a full dose, if there is no response, discuss discontinuing the drug with your doctor and trying another. You might also discuss with him or her the ideal time to take the medication. For example, some types of nerve pain often become worse at bedtime, so treatment during the day might not be necessary.

Bipolar disorder

The evidence for effectiveness in treating bipolar disorder is strongest for carbamazepine, valproic acid (and divalproex), lamotrigine, and oxcarbazepine.

Manic Phase

While response is variable among individual patients, in general, 40 to 70 percent of the people with bipolar disorder who take carbamazepine or valproic acid/divalproex can expect to experience a noticeable decrease in manic symptoms after about three weeks of treatment. Rates with oxcarbazepine are similar.

Depressive Phase

Lamotrigine is the only anticonvulsant proven effective in treating depressive episodes of bipolar disorder

and also as “maintenance therapy” to stabilize mood when taken for three weeks or longer. More than 50 percent of people experienced some benefit after taking the drug for seven weeks, with a reduction in both manic and depressive symptoms. But effectiveness falls off somewhat over the longer-term, with about a third (36 percent) of the people in one study staying “in remission” (with stabilized mood) a year and a half after treatment started.

Valproic acid/divalproex was less effective than lamotrigine, resulting in 40 percent of patients having meaningful reductions in depressive symptoms over six to eight weeks.

The treatment of so-called “rapid-cycling” bipolar disorder with anticonvulsants hasn’t been studied as much. While just over half of patients with rapid-cycling might respond to lamotrigine during acute treatment, it was not effective in preventing the need for additional treatments over six to eight months. In comparison, only one-quarter of the patients treated with combination valproic acid/divalproex and lithium had a response in acute treatment, but less than half had relapsed while taking either drug alone for up to 20 months.

Taking all the evidence into consideration, we chose the following as *Best Buys* for treating bipolar disorder if you and your doctor decide to try an anticonvulsant:

- *Generic carbamazepine, generic valproic acid, or generic divalproex*—for treating the manic phase of bipolar disorder
- *Generic lamotrigine*—for treating the depressive phase of bipolar disorder

Nerve pain

Three anticonvulsants—gabapentin (Neurontin), pregabalin (Lyrica), and lamotrigine (Lamictal)—have been well-studied in treating wide-spread nerve pain, while another three have limited evidence: carbamazepine (Tegretol), oxcarbazepine (Trileptal), and lacosamide (Vimpat). Those studies have focused mostly on nerve pain due to shingles and diabetes. For a more localized type of nerve pain—trigeminal neuralgia which affects nerves in

the face—carbamazepine (Tegretol) is the only anticonvulsant consistently shown to be effective. (See page 7 for information on these types of pain.)

Nerve Pain Due to Shingles and Diabetes

Consistent evidence supports the effectiveness of gabapentin and pregabalin (Lyrica) in treating shingles-related nerve pain (postherpetic neuralgia) and diabetic neuropathy, with no clear difference between the drugs in effect on pain.

Studies have found both drugs can yield pain relief within the first two weeks of treatment, a critical factor for people who experience the most intense episodes of nerve pain. In addition, studies show that both drugs improve sleep patterns and overall quality of life. Gabapentin has an advantage when it comes to price, however, because it is available as a less expensive generic formulation.

Treatment guidelines from the American Academy of Neurology (AAN) recommend pregabalin as the first-choice drug to treat diabetic nerve pain. But the AAN’s analysis left out 15 studies included in the evaluation conducted by the Drug Effectiveness Review Project (DERP) at the Oregon Health & Science University, which forms the basis of our report.

One of the studies not included in the AAN analysis was a trial that directly compared gabapentin and pregabalin, which found no difference between the drugs overall for treating diabetic nerve pain. DERP also analyzed the results of several studies together, which consistently showed no difference between the drugs for treating diabetic nerve pain.

While lamotrigine and lacosamide work better than a placebo to reduce pain, they are not superior to pregabalin or gabapentin.

No large-scale studies have evaluated any of the other anticonvulsants in treating nerve pain due to diabetes or shingles. And the findings of small studies of topiramate and oxcarbazepine are conflicting. Taking the study results together, topiramate was found to work better than a placebo in pain reduction but oxcarbazepine was not. But the studies so far are inconclusive. Only one older anticonvulsant—valproic acid/divalproex—has been studied in patients with diabetic neuropathy or

shingles-related nerve pain, and worked better than a placebo in small studies.

Facial Nerve Pain (Trigeminal Neuralgia)

Carbamazepine, which is FDA-approved for treating trigeminal neuralgia and is widely considered a first line treatment, has been proven effective in relieving the pain of this condition. About one in three people who have this form of nerve pain can expect good or complete relief, and another 40 percent will get some relief. But most patients require high doses, which raises the risk of side effects.

Oxcarbazepine has also been found effective and was tolerated better by patients in some studies.

Other Types of Pain

Certain anticonvulsants have been prescribed “off-label” for other types of nerve pain conditions, but the studies on those are small and don’t compare the drugs to other drug treatments, so the evidence is still not clear on how much they help.

Pregabalin and gabapentin have shown promise in treating other types of nerve pain, including pain associated with spinal cord injury, brain injury, and trauma. Pregabalin worked better than a placebo to reduce pain in patients following a stroke. Gabapentin has also been studied in complex regional pain syndrome, and phantom limb pain, and while pain scores were reduced more than with a placebo, there was no increase in the ability to function or improvements with quality of life. Levetiracetam was not superior to a placebo in reducing nerve pain following mastectomy.

Lamotrigine has shown promise in reducing pain in people with HIV who are taking neurotoxic antiretroviral drugs and in patients with pain following spinal cord injury or stroke. But gabapentin was not found to work better than a placebo in treating nerve pain in people with HIV who are taking neurotoxic antiretroviral drugs.

Fewer patients receiving a certain type of chemotherapy had nerve pain after completing therapy while taking oxcarbazepine than a placebo. Studies of lamotrigine and gabapentin used to treat nerve pain that developed while taking chemotherapy did not find the drugs to be effective.

Levetiracetam was better than a placebo in reducing nerve pain in patients with multiple sclerosis, while lamotrigine was not found to be better than a placebo.

The longer-term effectiveness of anticonvulsants in treating nerve pain of all sorts remains largely unknown. Most of the studies have lasted only one to two months and have focused on the measurement of pain relief using numerical rating scales. In addition, very few studies have evaluated whether anticonvulsants improve the overall quality of life. And no studies have directly compared the older and newer drugs for pain control.

Taking all the evidence into consideration, we chose the following as *Best Buys* for treating specific nerve-pain syndromes if you and your doctor decide to try an anticonvulsant:

- **Generic gabapentin**—for treating nerve pain due to shingles and diabetes
- **Generic carbamazepine**—for treating facial nerve pain (trigeminal neuralgia)

Fibromyalgia

Two anticonvulsant drugs—pregabalin (Lyrica) and gabapentin—have been studied and reduce pain in people with fibromyalgia. Pregabalin has a much larger evidence base, with 2,757 patients involved in four short-term studies that showed a modest reduction in pain, resulting in FDA approval for it to treat fibromyalgia. Overall, 42 percent more people achieve “response” (defined as experiencing a reduction in pain of 30 percent or more) with pregabalin compared to placebo over two to three months. (The rate of response in the pregabalin groups ranged from 38 to 50 percent compared to 28 percent for those taking a placebo.)

But the benefit of pregabalin might fade over time. In one study, people with fibromyalgia who experienced at least a 50 percent reduction in their pain after taking pregabalin for six weeks extended their time in the study, and took the medication for an additional six months. For about a third of those people, pregabalin continued to work, but only reduced pain by about 30 percent instead. The aver-

age time for this to happen was just over a month. No such studies have been done with gabapentin, so it's uncertain if its benefits also fade over time.

People who took pregabalin experienced feeling less fatigue for up to 15 weeks, but it wasn't sustained in longer studies and at higher doses. While pregabalin also reduced pain and improved the ability to function, it didn't improve a person's quality of life.

To date, gabapentin has been studied as a treatment for fibromyalgia only in 150 patients but 51 percent of them achieved "response"—a 64 percent increase over the 31 percent response rate in the placebo group. Gabapentin also improved sleep quality, and the overall effect of fibromyalgia (both pain and the

ability to function), but didn't improve the quality of life or depressive symptoms. While these results suggest that gabapentin might be more effective in reducing pain than pregabalin, there are no studies comparing the drugs with each other.

These drugs are important additions to the drug-treatment options for fibromyalgia. But you and your doctor should continue to weigh the pros and cons of all the treatment options for this condition.

Taking all the evidence into consideration, we chose the following as *Best Buys* for treating fibromyalgia if you and your doctor and you decide to try an anticonvulsant:

- *Generic gabapentin*

Table 1. Effectiveness of Selected Anticonvulsants*

Drug	Bipolar Disorder	Nerve Pain	Fibromyalgia
Carbamazepine	<ul style="list-style-type: none"> ■ Mood stabilization in manic episodes in 40 to 70 percent of the people in studies. 	<ul style="list-style-type: none"> ■ Very good results for relieving trigeminal neuralgia (intense facial pain); 75 percent get some relief and about one in three get almost complete pain relief. 	
Valproic Acid	<ul style="list-style-type: none"> ■ Clear improvement and moderate stabilization during manic episodes in 40 to 60 percent of the people in studies. ■ Combination with lithium might improve benefit during maintenance. ■ Might be useful in acute episodes of bipolar depression. 	<ul style="list-style-type: none"> ■ Pain relief in up to 60 percent of people with postherpetic pain in studies. 	
Oxcarbazepine	<ul style="list-style-type: none"> ■ As effective as valproic acid/divalproex and carbamazepine in treating manic episodes. 		
Gabapentin	<ul style="list-style-type: none"> ■ Not found to be effective in limited studies. 	<ul style="list-style-type: none"> ■ Strong results in treating postherpetic neuralgia, with one of every four patients having moderate overall improvement compared with some other anticonvulsants. ■ Moderate overall improvement in up to half of people with diabetic neuropathy within first 1-2 weeks. ■ Possible but still inconclusive effectiveness in treating spinal cord injury pain, HIV-related neuropathy, and neuropathic cancer pain. 	<ul style="list-style-type: none"> ■ In one study of 150 people, about half of patients taking gabapentin experienced relief from pain. ■ Other symptoms also improved in the short-term. ■ How long the pain relief lasts is unknown.
Pregabalin (Lyrica)	No evidence.	<ul style="list-style-type: none"> ■ Pain relief in 28 to 58 percent of people with postherpetic neuralgia. ■ Pain relief in 40 to 48 percent of patients with diabetic neuropathy. 	<ul style="list-style-type: none"> ■ 38 to 50 percent of patients experience pain relief in short-term, but the benefit was lost over the following 6 months in as many as one-third of responders. ■ Fatigue improved in the short-term but not the long-term.

Table 1. Effectiveness of Selected Anticonvulsants* (continued)

Drug	Bipolar Disorder	Nerve Pain	Fibromyalgia
Lamotrigine	<ul style="list-style-type: none"> Remission from depressed episodes lasting at least seven months in one key study. 	<ul style="list-style-type: none"> Possible effectiveness for relieving nerve pain that follows a stroke. Possible effectiveness for relieving pain associated with trigeminal neuralgia. 	
Phenytoin	<ul style="list-style-type: none"> Insufficient evidence to make conclusions. 		
Topiramate	<ul style="list-style-type: none"> Not found to be effective in limited studies. 	<ul style="list-style-type: none"> Some evidence for effectiveness in treating diabetic neuropathy, with 36 percent of patients experiencing obvious pain relief. 	

* Results presented are based on results from several studies.

Side Effects and Safety Issues with Anticonvulsants

All anticonvulsants can cause side effects. Between 44 and 95 percent of the people taking them experience at least one. The most common are dizziness, sleepiness, and nausea. Some of the newer anticonvulsants cause swelling of hands and feet, weight gain, blurry vision, trouble concentrating, and memory lapses.

Most people who start taking an anticonvulsant continue on the medicine. But the rate of people who stop taking the medicine is different for each drug (see Table 2 on page 15). How many people stop taking a drug is considered a good barometer of how well it is tolerated over time.

Some anticonvulsants have been linked to serious adverse effects, including suicide, life-threatening skin rashes and fatal liver failure. All of them might cause birth defects, so they should not be taken by pregnant women or women who plan to become pregnant. See Table 2 on the next page for the side effects associated with particular anticonvulsants.

Anticonvulsants are often taken with other drugs, and two anticonvulsants are sometimes taken together. This requires extra vigilance on your part and that of your doctor. Always be sure to tell your doctor about all the other prescription drugs, supplements, and over-the-counter medications you are taking.

The newer anticonvulsants are sometimes thought to be safer, with fewer side effects than the older ones. No large, good quality studies have tested this directly, but small, short-term studies that compared the drugs don't support such a conclusion. The types of side effects and safety issues differ between the older and newer drugs, but drugs within each group also pose different risks. Your doctor should assess your individual circumstances.

Table 2. Side Effects and Safety Profile of Selected Anticonvulsants

Drug	Rate that people stopped taking the drug*	Serious Side Effects	Common Side Effects
Carbamazepine	9-13%	<ul style="list-style-type: none"> ■ Rare risk of drop in blood cell and platelet counts and liver failure. ■ Less suitable for people with a history of bone marrow deficiencies or liver disease. ■ Risk of life-threatening rashes, including Stevens-Johnson Syndrome (1-6 cases per 1,000 patients). Patients of Asian origin are at higher risk and require genetic tests before starting therapy. ■ Any rash while taking should prompt immediate contact with your doctor. ■ Should not be taken by pregnant women or women who may become pregnant because it can cause birth defects. 	<ul style="list-style-type: none"> ■ Dizziness is the most common side effect in the early phase of taking this medication. Other side effects include drowsiness, unsteadiness, nausea, and vomiting. ■ Requires monitoring drug level in the blood.
Divalproex, Valproic Acid	4-11%	<ul style="list-style-type: none"> ■ Linked to rare cases of fatal liver failure and life-threatening pancreatitis, especially when taken by young children. As a result, periodic liver-function tests required for people of all ages. ■ Prolonged or severe abdominal pain while taking should prompt immediate visit to a doctor. ■ Should not be taken by pregnant women or women who plan to become pregnant. Linked to rare cases of birth defects. ■ Seriously low platelet levels in more than 20 percent of patients, and related to higher doses. Blood level monitoring recommended. 	<ul style="list-style-type: none"> ■ Dizziness, drowsiness, hair loss, nausea, tremor, vomiting, weight gain or weight loss are most common. ■ Periodic monitoring of blood level of the drug is recommended. ■ Interactions with other drugs might increase or decrease blood levels.
Gabapentin	5-19%	<ul style="list-style-type: none"> ■ Some children experience emotional problems—uncontrollable, exaggerated emotional responses, such as laughing or crying—hostility, including aggressive behavior; thought disorder, including concentration problems and changes in school performance; and restlessness and hyperactivity. ■ Should not be taken by pregnant women or women who plan to become pregnant, due to risk of birth defects. 	<ul style="list-style-type: none"> ■ Dizziness, drowsiness, edema, headache, and weight gain. ■ Use cautiously in patients with pre-existing heart failure. ■ Also more common: nausea, sedation, lightheadedness, and insomnia.

Table 2. Side Effects and Safety Profile of Selected Anticonvulsants (continued)

Drug	Rate that people stopped taking the drug*	Serious Side Effects	Common Side Effects
Lamotrigine	1%-30%	<ul style="list-style-type: none"> ■ Risk of life-threatening rashes, including Stevens-Johnson Syndrome. Risk is highest in children (8 cases per 1,000 patients) and decreases sharply with age. Risk is higher with larger doses and a rapid increase in dose. ■ Should not be taken by pregnant women or women who plan to become pregnant, because of the risk of birth defects including cleft lip and cleft palate. ■ Rare risk of drop in blood-cell and platelet counts. 	<ul style="list-style-type: none"> ■ Nausea, insomnia, somnolence, back pain, fatigue, rash, and rhinitis. ■ Periodic monitoring of blood level of the drug is recommended.
Oxcarbazepine	9%-23%	<ul style="list-style-type: none"> ■ Rare but serious low sodium in the blood (2.5 percent of people). ■ Rare first-dose anaphylactic reactions, including swelling of the tongue, lips, and throat. ■ Risk of life-threatening rashes, including Stevens-Johnson Syndrome. Risk is higher with larger doses and a rapid increase in dose. ■ Should not be taken by pregnant women or women who plan to become pregnant due to the potential risk of birth defects. ■ 25 to 30 percent of patients who have had allergic reactions to carbamazepine will also have such reactions to oxcarbazepine. ■ Rare risk of drop in blood cell and platelet counts. 	<ul style="list-style-type: none"> ■ Dizziness, double-vision, drowsiness, fatigue, nausea, and vomiting. ■ Other side effects are difficulty with concentration, speech or language problems, and coordination problems.
Pregabalin (Lyrica)	11%-32%	<ul style="list-style-type: none"> ■ Rare first-dose anaphylactic reactions, including swelling of the tongue, lips and throat. ■ Allergic reactions (e.g. hives, difficulty breathing, and wheezing) can occur. ■ Should not be taken by pregnant women or women who plan to become pregnant, due to risk of birth defects. 	<ul style="list-style-type: none"> ■ Dizziness, drowsiness, edema, headache, weight gain. Due to potential edema, use cautiously in patients with pre-existing heart failure. ■ Also more common: dry mouth, vision problems, and difficulty concentrating.

Table 2. Side Effects and Safety Profile of Selected Anticonvulsants (continued)

Drug	Rate that people stopped taking the drug*	Serious Side Effects	Common Side Effects
Topiramate	24%	<ul style="list-style-type: none"> ■ Heightened risk of kidney stones or development of abnormal skin sensations (paresthesia); extra water consumption is strongly urged. ■ Greater risk of weight loss (19 to 38 percent of patients) than other anticonvulsants. ■ Glaucoma ■ Can reduce effectiveness of oral contraceptives. ■ Interacts with multiple other drugs. ■ Should not be used by pregnant women or women who plan to become pregnant. It has been linked to birth defects in animal studies. 	<ul style="list-style-type: none"> ■ Other common side effects include: anorexia, confusion, dizziness, difficulty concentrating, drowsiness, fatigue, memory problems, nervousness.

* Range based on data from multiple studies. Withdrawal means a person stopped taking the drug and does not intend to start taking it again.

Other Serious Side Effects

All anticonvulsants	Antiepileptic drugs (AEDs) increase the risk of suicidal thoughts or behavior in people taking them for any indication.
Carbamazepine, divalproex/valproic acid, lamotrigine, oxcarbazepine	Although rare, serious and life-threatening multi-organ hypersensitivity might occur during the first two weeks of treatment. Symptoms are diverse but include multiple organ systems.

Table 3. The Anticonvulsants – Dosing and Costs

The older drugs are in italics in first column. The newer ones are in regular text.

Note: If the price box contains a **\$**, that indicates the dose of that drug is likely available for a low monthly cost through discount programs offered by large chain stores. For example, Kroger, Sam's Club, Target, and Walmart offer a month's supply of selected generic drugs for \$4 or a three-month supply for \$10. Other chain stores, such as Costco, CVS, Kmart, and Walgreens, offer similar programs. Some programs have restrictions or membership fees, so check the details carefully for restrictions and to make sure your drug is covered.

	Generic Name and Dose	Brand Name ¹	Number of Pills Per Day ²	Total Daily Dose ³	Average Monthly Cost ⁴
	<i>Carbamazepine 100 mg chewable tablet</i>	Tegretol	Three	300 mg	\$75
CR BEST BUY	<i>Carbamazepine 100 mg chewable tablet</i>	Generic	Three	300 mg	\$21 \$
	<i>Carbamazepine 200 mg tablet</i>	Epitol	Three	600 mg	\$15
	<i>Carbamazepine 200 mg tablet</i>	Tegretol	Three	600 mg	\$115
CR BEST BUY	<i>Carbamazepine 200 mg tablet</i>	Generic	Three	600 mg	\$19 \$
	<i>Carbamazepine 100 mg SR tablet⁵</i>	Carbatrol	Two	200 mg	\$134
	<i>Carbamazepine 100 mg SR tablet</i>	Tegretol XR	Two	200 mg	\$42
	<i>Carbamazepine 200 mg SR tablet</i>	Carbatrol	Two	400 mg	\$133
	<i>Carbamazepine 200 mg SR tablet</i>	Tegretol XR	Two	400 mg	\$79
CR BEST BUY	<i>Carbamazepine 200 mg SR tablet</i>	Generic	Two	400 mg	\$58
	<i>Carbamazepine 300 mg SR tablet</i>	Carbatrol	Two	600 mg	\$133
	<i>Carbamazepine 400 mg SR tablet</i>	Tegretol XR	Two	800 mg	\$145
CR BEST BUY	<i>Carbamazepine 400 mg SR tablet</i>	Generic	Two	800 mg	\$112
	<i>Divalproex 125 mg tablet</i>	Depakote	Three	375 mg	\$140
CR BEST BUY	<i>Divalproex 125 mg tablet</i>	Generic	Three	375 mg	\$66
	<i>Divalproex 125 mg capsule</i>	Depakote Sprinkle	Three	375 mg	\$134
CR BEST BUY	<i>Divalproex 125 mg capsule</i>	Generic	Three	375 mg	\$75
	<i>Divalproex 250 mg tablet</i>	Depakote	Three	750 mg	\$242
CR BEST BUY	<i>Divalproex 250 mg tablet</i>	Generic	Three	750 mg	\$108
	<i>Divalproex 500 mg tablet</i>	Depakote	Three	1,500 mg	\$433
CR BEST BUY	<i>Divalproex 500 mg tablet</i>	Generic	Three	1,500 mg	\$187
	<i>Divalproex 250 mg SR tablet</i>	Depakote ER	One	250 mg	\$79
CR BEST BUY	<i>Divalproex 250 mg SR tablet</i>	Generic	One	250 mg	\$42
	<i>Divalproex 500 mg SR tablet</i>	Depakote ER	One	500 mg	\$123
CR BEST BUY	<i>Divalproex 500 mg SR tablet</i>	Generic	One	500 mg	\$66
	<i>Gabapentin 100 mg capsule</i>	Neurontin	Three	300 mg	\$99
CR BEST BUY	<i>Gabapentin 100 mg capsule</i>	Generic	Three	300 mg	\$33 \$
CR BEST BUY	<i>Gabapentin 100 mg tablet</i>	Generic	Three	300 mg	\$46
	<i>Gabapentin 300 mg capsule</i>	Neurontin	Three	900 mg	\$217

Table 3. The Anticonvulsants – Dosing and Costs (continued)

The older drugs are in italics in first column. The newer ones are in regular text.

	Generic Name and Dose	Brand Name ¹	Number of Pills Per Day ²	Total Daily Dose ³	Average Monthly Cost ⁴
CR BEST BUY	Gabapentin 300 mg capsule	Generic	Three	900 mg	\$68
	Gabapentin 400 mg capsule	Neurontin	Three	1,200 mg	\$257
CR BEST BUY	Gabapentin 400 mg capsule	Generic	Three	1,200 mg	\$82
CR BEST BUY	Gabapentin 400 mg tablet	Generic	Three	1,200 mg	\$119
	Gabapentin 600 mg tablet	Neurontin	Three	1,800 mg	\$396
CR BEST BUY	Gabapentin 600 mg tablet	Generic	Three	1,800 mg	\$134
	Gabapentin 800 mg tablet	Neurontin	Three	2,400 mg	\$462
CR BEST BUY	Gabapentin 800 mg tablet	Generic	Three	2,400 mg	\$145
	Lamotrigine 25 mg tablet	Lamictal	One	25 mg	\$196
CR BEST BUY	Lamotrigine 25 mg tablet	Generic	One	25 mg	\$92
	Lamotrigine 25 mg dissolvable tablet	Lamictal ODT	One	25 mg	\$186
	Lamotrigine 25 mg SR tablet	Lamictal XR	One	25 mg	\$177
	Lamotrigine 50 mg dissolvable tablet	Lamictal ODT	One	50 mg	\$200
	Lamotrigine 50 mg SR tablet	Lamictal XR	One	50 mg	\$368
	Lamotrigine 100 mg tablet	Lamictal	One	100 mg	\$212
CR BEST BUY	Lamotrigine 100 mg tablet	Generic	One	100 mg	\$106
	Lamotrigine 100 mg dissolvable tablet	Lamictal ODT	One	100 mg	\$213
	Lamotrigine 100 mg SR tablet	Lamictal XR	One	100 mg	\$378
	Lamotrigine 150 mg tablet	Lamictal	One	150 mg	\$221
CR BEST BUY	Lamotrigine 150 mg tablet	Generic	One	150 mg	\$118
	Lamotrigine 200 mg tablet	Lamictal	One	200 mg	\$255
CR BEST BUY	Lamotrigine 200 mg tablet	Generic	One	200 mg	\$122
	Lamotrigine 200 mg dissolvable tablet	Lamictal ODT	One	200 mg	\$256
	Lamotrigine 200 mg SR tablet	Lamictal XR	One	200 mg	\$400
	Levetiracetam 250 mg tablet	Keppra	Two	500 mg	\$327
	Levetiracetam 250 mg tablet	Generic	Two	500 mg	\$109
	Levetiracetam 500 mg tablet	Keppra	Two	1,000 mg	\$382
	Levetiracetam 500 mg tablet	Generic	Two	1,000 mg	\$127
	Levetiracetam 500 mg SR tablet	Keppra XR	One	500 mg	\$173
	Levetiracetam 750 mg tablet	Keppra	Two	1,500 mg	\$560
	Levetiracetam 750 mg tablet	Generic	Two	1,500 mg	\$174
	Levetiracetam 750 mg SR tablet	Keppra XR	One	750 mg	\$232

Table 3. The Anticonvulsants – Dosing and Costs (continued)

The older drugs are in italics in first column. The newer ones are in regular text.

Generic Name and Dose	Brand Name ¹	Number of Pills Per Day ²	Total Daily Dose ³	Average Monthly Cost ⁴
Levetiracetam 1,000 mg tablet	Keppra	Two	2,000 mg	\$766
Levetiracetam 1,000 mg tablet	Generic	Two	2,000 mg	\$289
Oxcarbazepine 150 mg tablet	Trileptal	Two	300 mg	\$172
Oxcarbazepine 150 mg tablet	Generic	Two	300 mg	\$74
Oxcarbazepine 300 mg tablet	Trileptal	Two	600 mg	\$287
Oxcarbazepine 300 mg tablet	Generic	Two	600 mg	\$125
Oxcarbazepine 600 mg tablet	Trileptal	Two	1,200 mg	\$505
Oxcarbazepine 600 mg tablet	Generic	Two	1,200 mg	\$208
<i>Phenytoin 30 mg ER capsule⁶</i>	Dilantin	Three	90 mg	\$63
<i>Phenytoin 50 mg chewable tablet</i>	Dilantin	Three	150 mg	\$74
<i>Phenytoin 100 mg ER capsule</i>	Dilantin	Three	300 mg	\$56
<i>Phenytoin 100 mg ER capsule</i>	Generic	Three	300 mg	\$27
<i>Phenytoin 200 mg ER capsule</i>	Phenytek	Two	400 mg	\$76
<i>Phenytoin 200 mg ER capsule</i>	Generic	Two	400 mg	\$60
<i>Phenytoin 300 mg ER capsule</i>	Phenytek	One	300 mg	\$59
<i>Phenytoin 300 mg ER capsule</i>	Generic	One	300 mg	\$42
Pregabalin 25 mg capsule	Lyrica	Three	75 mg	\$310
Pregabalin 50 mg capsule	Lyrica	Three	150 mg	\$299
Pregabalin 75 mg capsule	Lyrica	Three	225 mg	\$300
Pregabalin 100 mg capsule	Lyrica	Three	300 mg	\$307
Pregabalin 150 mg capsule	Lyrica	Three	450 mg	\$303
Pregabalin 200 mg capsule	Lyrica	Three	600 mg	\$306
Pregabalin 225 mg capsule	Lyrica	Two	450 mg	\$208
Pregabalin 300 mg capsule	Lyrica	One	300 mg	\$103
Tiagabine 2 mg tablet	Gabitril	Three	6 mg	\$508
Tiagabine 4 mg tablet	Gabitril	Three	12 mg	\$513
Tiagabine 12 mg tablet	Gabitril	Three	36 mg	\$669
Tiagabine 16 mg tablet	Gabitril	Three	48 mg	\$866
Topiramate 15 mg capsule	Topamax	Two	30 mg	\$247
Topiramate 15 mg capsule	Generic	Two	30 mg	\$133
Topiramate 25 mg tablet	Topamax	Two	50 mg	\$245
Topiramate 25 mg tablet	Generic	Two	50 mg	\$102

Table 3. The Anticonvulsants – Dosing and Costs (continued)

The older drugs are in italics in first column. The newer ones are in regular text.

Generic Name and Dose	Brand Name ¹	Number of Pills Per Day ²	Total Daily Dose ³	Average Monthly Cost ⁴
Topiramate 25 mg capsule	Topamax	Two	50 mg	\$315
Topiramate 25 mg capsule	Generic	Two	50 mg	\$158
Topiramate 50 mg tablet	Topamax	Two	100 mg	\$445
Topiramate 50 mg tablet	Generic	Two	100 mg	\$207
Topiramate 100 mg tablet	Topamax	Two	200 mg	\$625
Topiramate 100 mg tablet	Generic	Two	200 mg	\$303
Topiramate 200 mg tablet	Topamax	Two	400 mg	\$762
Topiramate 200 mg tablet	Generic	Two	400 mg	\$387
<i>Valproic Acid 250 mg capsule</i>	Generic	Three	750 mg	\$41
<i>Valproic Acid 250 mg delayed release capsule</i>	Stavzor	Three	750 mg	\$233
<i>Valproic Acid 500 mg delayed release capsule</i>	Stavzor	Three	1,500 mg	\$413
Zonisamide 25 mg capsule	Zonegran	One	25 mg	\$37
Zonisamide 25 mg capsule	Generic	One	25 mg	\$14 
Zonisamide 50 mg capsule	Generic	One	50 mg	\$19
Zonisamide 100 mg capsule	Zonegran	One	100 mg	\$135
Zonisamide 100 mg capsule	Generic	One	100 mg	\$31

1. "Generic" indicates that this is the generic version of this drug at the dose given.

2. Reflects typical or commonly recommended dosing. Many of the anticonvulsants are prescribed at widely varying doses that might be less than or greater than the range indicated in this table. With many drugs in this table, it's also common to start at a lower dose for two weeks or more and increase it over the next few weeks. Many of the drugs are ineffective or only marginally effective at a low dose.

3. See note 2.

4. Prices reflect nationwide retail averages for April 2011. They are rounded to the nearest dollar. Information is derived by *Consumer Reports Health Best Buy Drugs* from data provided by Wolters Kluwer Pharma Solutions, which is not involved in our analysis or recommendations.

5. SR=Sustained release

6. ER=Extended release

Talking With Your Doctor

It's important for you to know that the information we present in this report is not meant to substitute for a doctor's judgment. But we hope it will help you and your doctor arrive at a decision about which anticonvulsant is best for you, if one is warranted, and which will give you the most value for your health-care dollar.

Bear in mind that many people are reluctant to discuss the cost of medicines with their doctors. Also, studies have found that doctors do not routinely take price into account when prescribing medicines. So unless you bring it up, your doctor might assume that cost is not a factor for you.

Many people (including physicians) think that newer drugs are better. While that's a natural assumption to make, it's not necessarily true. Studies consistently find that many older medicines are as good as—and in some cases better than—newer medicines. Certain older drugs can be thought of as "tried and true," particularly when it comes to their safety record. Newer drugs have not yet met the test of time, and unexpected problems can and do crop up once they hit the market.

Of course, some newer drugs are indeed more effective and safer. Talk with your doctor about the pluses and minuses of newer vs. older medicines, including generic drugs.

Prescription medicines go "generic" when a company's patents on them lapse, usually after about 12 to 15 years. At that point, other companies can make and sell the drug.

Generics are almost always much less expensive than newer brand-name medicines, but they are not lesser quality drugs. Indeed, most generics remain useful medicines even many years after first being marketed. That is why more than 60 percent of all prescriptions in the U.S. today are for generics.

Another important issue to talk with your doctor about is keeping a record of the drugs you are taking. There are several reasons for this:

- First, if you see several doctors, they might not be aware of medicines the others have prescribed for you.
- Second, since people differ in their response to medications, it is very common for doctors today to prescribe several medicines for a person before finding one that works well or best.
- Third, many people take several prescription medications, nonprescription drugs, and dietary supplements at the same time. They can interact in ways that can either reduce the benefit you get from the drugs or be dangerous.
- Fourth, the names of prescription drugs—both generic and brand—are often difficult to pronounce and remember.

For all these reasons, it's important to keep a written list of all the drugs and supplements you are taking, and to periodically review it with your doctors.

And always be sure that you understand the dose of the medicine being prescribed and how many pills you are expected to take each day. Your doctor should tell you this information. When you fill a prescription at a pharmacy or get it by mail, make sure the dose and the number of pills per day on the container match the amount your doctor told you to take.

How We Picked the *Best Buy* Anticonvulsants

Our evaluation is based on an independent scientific review of the evidence on the effectiveness, safety, and adverse effects of anticonvulsants. A team of physicians and researchers at the Oregon Health & Science University Evidence-Based Practice Center conducted the analysis as part of the Drug Effectiveness Review Project, or DERP. DERP is a first-of-its-kind 12-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP's analysis of anticonvulsants forms the basis for this report. A consultant to *Consumers Reports Health Best Buy Drugs* is also a member of the Oregon-based research team, which has no financial interest in any pharmaceutical company or product.

The full DERP review of anticonvulsant drugs is available at <http://www.ohsu.edu/drugeffectiveness/reports/final.cfm>. (Note: This is a long and technical document written for physicians.)

The prescription drug costs we cite were obtained from a health-care information company that tracks sales of prescription drugs in the U.S. Prices

for a drug can vary quite widely, even within a city or town. All the prices in this report are national averages based on sales of prescription drugs in retail outlets. They reflect the cash price paid for a month's supply of each drug in April 2011.

Consumers Union and *Consumer Reports* selected the *Best Buy Drugs* using the following criteria. The drug had to:

- Be as effective or more effective than other anticonvulsants
- Have a safety record equal to or better than other anticonvulsants
- Be priced reasonably compared with other anticonvulsants or deliver value for the money if it was a relatively costly medicine

The *Consumers Reports Health Best Buy Drugs* methodology is described in more detail in the methods section at ConsumerReportsHealth.org/BestBuyDrugs.

Using and Sharing this Report

This copyrighted report can be freely downloaded, reprinted, and disseminated for individual noncommercial use without permission from Consumers Union or *Consumer Reports*® magazine as long as it's clearly attributed to *Consumer Reports Health Best Buy Drugs*™. We encourage its wide dissemination as well for the purpose of informing consumers. But Consumers Union does not authorize the use of its name or materials for commercial,

marketing, or promotional purposes. Any organization interested in broader distribution of this report should contact wintwe@consumer.org. *Consumer Reports Health Best Buy Drugs*™ is a trademark of Consumers Union of U.S., Inc. All quotes from the material should cite *Consumer Reports Health Best Buy Drugs*™ as the source.

© *Consumers Union of U.S., Inc.* 2011

About Us

Consumers Union, publisher of *Consumer Reports*® magazine, is an independent and nonprofit organization whose mission since 1936 has been to provide consumers with unbiased information on goods and services and create a fair marketplace. Its website is www.consumersunion.org. The magazine's website is www.consumerreports.org.

Consumer Reports Health Best Buy Drugs™ is a public education project administered by Consumers Union. These materials are made possible from a grant by the state Attorney General Consumer and Prescriber Education Grant Program, which is funded by the multi-state settlement of consumer-fraud claims regarding the marketing of the prescription drug Neurontin.

The Engelberg Foundation provided a major grant to fund the creation of the project from 2004 to 2007. Additional initial funding came from the National Library of Medicine, part of the National Institutes of Health. A more detailed explanation of the

project is available at ConsumerReportsHealth.org/BestBuyDrugs.

We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Health Best Buy Drugs* website is accurate and describes generally accepted clinical practices. If we find an error or are alerted to one, we will correct it as quickly as possible. But Consumer Reports and its authors, editors, publishers, licensors, and suppliers cannot be responsible for medical errors or omissions, or any consequences from the use of the information on this site. Please refer to our user agreement at ConsumerReportsHealth.org/BestBuyDrugs for further information.

Consumer Reports Health Best Buy Drugs should not be viewed as a substitute for a consultation with a medical or health professional. This report and the information on ConsumerReportsHealth.org/BestBuyDrugs are provided to enhance your communication with your doctor rather than to replace it.

References

- Obrocea G.V. et al. "Clinical predictors of response to lamotrigine and gabapentin monotherapy in refractory affective disorders." *Biological Psychiatry* 2002; 51(3):253-60.
- Frye M.A. et al. "A placebo-controlled study of lamotrigine and gabapentin monotherapy in refractory mood disorders." *Journal of Clinical Psychopharmacology* 2000; 20(6):607-14.
- Tohen M. et al. "Olanzapine versus divalproex sodium for the treatment of acute mania and maintenance of remission: a 47-week study." *Am J Psychiatry* 2003; 160(7):1263-71.
- Bowden C.L. et al. "A randomized, placebo-controlled 12-month trial of divalproex and lithium in treatment of outpatients with bipolar I disorder. Divalproex Maintenance Study Group." *Archives of General Psychiatry* 2000; 57:481-9.
- Lusznat R.M. et al. "Carbamazepine vs. lithium in the treatment and prophylaxis of mania." *British Journal of Psychiatry* 1988; 153:198-204.
- Greil W. et al. "Lithium versus carbamazepine in the maintenance treatment of bipolar disorders—a randomised study." *J Affect Disord* 1997; 43(2):151-61.
- Lerer B. et al. "Carbamazepine versus lithium in mania: a double-blind study." *Journal of Clinical Psychiatry* 1987; 48(3):89-93.
- Coxhead N. et al. "Carbamazepine versus lithium in the prophylaxis of bipolar affective disorder." *Acta Psychiatr Scand* 1992; 85(2):114-8.
- Denicoff K.D. et al. "Comparative prophylactic efficacy of lithium, carbamazepine, and the combination in bipolar disorder." *Journal of Clinical Psychiatry* 1997; 58(11):470-8.
- Zajacka J.M. et al. "A comparison of the efficacy, safety, and tolerability of divalproex sodium and olanzapine in the treatment of bipolar disorder." *Journal of Clinical Psychiatry* 2002; 63(12):1148-55.
- Bowden C.L. et al. "A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently manic or hypomanic patients with bipolar I disorder." *Archives of General Psychiatry* 2003; 60(4):392-400.
- Mishory A. et al. "Prophylactic effect of phenytoin in bipolar disorder: A controlled study." *Bipolar Disorders* 2003; 5(6): 464-467.
- Hartong E.G. et al. "Prophylactic efficacy of lithium versus carbamazepine in treatment-naïve bipolar patients." *J Clin Psychiatry* 2003; 64(2):144-51.
- Salloum I.M. et al. "Efficacy of valproate maintenance in patients with bipolar disorder and alcoholism: A double-blind placebo-controlled study." *Archives of General Psychiatry* 2005; 62(1):37-45.
- Vasudev K. et al. "Carbamazepine and valproate monotherapy: feasibility, relative safety and efficacy, and therapeutic drug monitoring in manic disorder." *Psychopharmacology* 2000; 150:15-23.
- Small J.G. et al. "Carbamazepine compared with lithium in the treatment of mania." *Archives of General Psychiatry* 1991; 48(10):915-21.
- Kleindienst N, Greil W. Inter-episodic morbidity and drop-out under carbamazepine and lithium in the maintenance treatment of bipolar disorder. *Psychological Medicine* 2002; 32(3):493-501.
- Greil W. et al. "Differential response to lithium and carbamazepine in the prophylaxis of bipolar disorder." *Journal of Clinical Psychopharmacology* 1998; 18(6):455-60.
- Gyulai L. et al. "Maintenance efficacy of divalproex in the prevention of bipolar depression." *Neuropsychopharmacology* 2003; 28(7):1374-82.
- Okuma T. et al. "Comparison of the antimanic efficacy of carbamazepine and lithium carbonate by double-blind controlled study." *Pharmacopsychiatry* 1990; 23(3):143-50.
- Calabrese J.R. et al. "A double-blind, placebo-controlled, prophylaxis study of lamotrigine in rapid-cycling bipolar disorder. Lamictal 614 Study Group." *J Clin Psychiatry* 2000; 61(11):841-50.
- Davis L.L. et al. "Divalproex in the treatment of bipolar depression: A placebo-controlled study." *Journal of Affective Disorders* 2005; 85(3):259-266.
- McIntyre RS, Mancini DA, McCann S, et al. Topiramate versus bupropion SR when added to mood stabilizer therapy for the depressive phase of bipolar disorder: a preliminary single-blind study. *Bipolar Disorders* 2002; 4(3): 207-13.
- Solomon D.A. et al. "A pilot study of lithium carbonate plus divalproex sodium for the continuation and maintenance treatment of patients with bipolar I disorder." *Journal of Clinical Psychiatry* 1997; 58(3):95-9.
- Pande A.C. et al. "Gabapentin in bipolar disorder: a placebo-controlled trial of adjunctive therapy." *Gabapentin Bipolar Disorder Study Group. Bipolar Disorders* 2000; 2(3 Pt 2):249-55.
- Calabrese J.R. et al. "A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently depressed patients with bipolar I disorder." *J Clin Psychiatry* 2003; 64(9):1013-24.
- Lechin F. et al. "Pimozide therapy for trigeminal neuralgia." *Archives of Neurology* 1989; 46:960-3.
- Skelton W.P. "Neuroleptics in painful thiamine deficiency neuropathy." *Southern Medical Journal* 1991; 84:1362-3.
- Gilron I. et al. "Morphine, gabapentin, or their combination for neuropathic pain." *New England Journal of Medicine* 2005; 352(13):1324-1334.
- Otto M. et al. "Valproic acid has no effect on pain in polyneuropathy: a randomized, controlled trial." *Neurology* 2004; 62(2):285-8.
- Van de Vusse A.C. et al. "Randomised controlled trial of gabapentin in Complex Regional Pain Syndrome type 1." *BMC Neurology* 2004; 4(-):9p
- Kochar D.K. et al. "Divalproex sodium in the management of post-herpetic neuralgia: A randomized double-blind placebo-controlled study." *QJM -Monthly Journal of the Association of Physicians* 2005; 98(1):29-34.
- Morello C.M. et al. "Randomized double-blind study comparing the efficacy of gabapentin with amitriptyline on diabetic peripheral neuropathy pain." *Arch Intern Med* 1999; 159(16):1931-7.
- Gomez-Perez F.J. et al. "Nortriptyline-fluphenazine vs. carbamazepine in the symptomatic treatment of diabetic neuropathy." *Archives of Medical Research* 1996; 27(4):525-9.
- Lindstrom P. et al. "The analgesic effect of tocainide in trigeminal neuralgia." *Pain* 1987; 28: 45-50.
- Leijon G. et al. "Central post-stroke pain—a controlled trial of amitriptyline and carbamazepine." *Pain* 1989; 36 (1):27-36.
- Tai Q. et al. "Gabapentin in the treatment of neuropathic pain after spinal cord injury: a prospective, randomized, double-blind, crossover trial." *Journal of Spinal Cord Medicine* 2002; 25(2):100-5.
- Harke H. et al. "The response of neuropathic pain and pain in complex regional pain syndrome I to carbamazepine and sustained-release morphine in patients pretreated with spinal cord stimulation: a double-blinded randomized study." *Anesthesia & Analgesia* 2001; 92(2):488-95.
- Campbell F.G. et al. "Clinical trial of carbamazepine (tegretol) in trigeminal neuralgia." *Journal of Neurology, Neurosurgery & Psychiatry* 1966; 29:265-7.
- Nicol CF. "A four year double-blind study of tegretol in facial pain." *Headache* 1969; 9:54-7.
- Drewes A.M. et al. "Valproate for treatment of chronic central pain after spinal cord injury. A double-blind cross-over study." *Paraplegia* 1994; 32(8):565-9.
- Finnerup N.B. et al. "Lamotrigine in spinal cord injury pain: a randomized controlled trial." *Pain* 2002; 96(3):375-83.
- McCleane G. "200 mg daily of lamotrigine has no analgesic effect in neuropathic pain: a randomized, double-blind, placebo controlled trial." *Pain* 1999; 83(1):105-7.
- Zakrzewska J.M. et al. "Lamotrigine (lamictal) in refractory trigeminal neuralgia: results from a double-blind placebo controlled crossover trial." *Pain* 1997; 73(2):223-30.
- Vestergaard K. et al. "Lamotrigine for central poststroke pain: a randomized controlled trial." *Neurology* 2001; 56(2):184-90.
- Kochar D.K. et al. "Sodium valproate for painful diabetic neuropathy: a randomized double-blind placebo-controlled study." *QJM* 2004; 97(1):33-8.
- Kochar D.K. et al. "Sodium valproate in the management of painful neuropathy in type 2 diabetes - a randomized placebo controlled study." *Acta Neurologica Scandinavica* 2002; 106(5):248-52.
- Chadda V.S. et al. "Double blind study of the effects of diphenylhydantoin sodium on diabetic neuropathy." *J Assoc Physicians India* 1978; 26(5):403-6.
- Rull J.A. et al. "Symptomatic treatment of peripheral diabetic neuropathy with carbamazepine (Tegretol): double blind crossover trial." *Diabetologia* 1969; 5(4):215-8.
- Eisenberg E. et al. "Lamotrigine reduces painful diabetic neuropathy: a randomized, controlled study." *Neurology* 2001; 57(3):505-9.
- Saudek C.D. et al. "Phenytoin in the treatment of diabetic symmetrical polyneuropathy." *Clinical Pharmacology & Therapeutics* 1977; 22:196-9.
- Dalesio D. "Medical treatment of tic douloureux." *Journal of Chronic Diseases* 1966; 19(10):1043-8.
- Luria Y. et al. "Lamotrigine in the treatment of painful diabetic neuropathy: A randomized, placebo-controlled study." *Progress in Pain Research and Management* 2000; 16:857-62.
- Simpson D.A. "Gabapentin and venlafaxine for the treatment of painful diabetic neuropathy." *Journal of Clinical Neuromuscular Disease* 2001; 3:53-62.

- Hahn K. et al. "A placebo-controlled trial of gabapentin for painful HIV-associated sensory neuropathies." *Journal of Neurology* 2004; 251(10):1260-1266.
- Levendoglu F. et al. "Gabapentin Is a First Line Drug for the Treatment of Neuropathic Pain in Spinal Cord Injury." *Spine* 2004; 29(7):743-751.
- Simpson D.M. et al. "A placebo-controlled trial of lamotrigine for painful HIV-associated neuropathy." *Neurology* 2000; 54(11):2115-9.
- Gorson K.C. et al. "Gabapentin in the treatment of painful diabetic neuropathy: a placebo controlled, double blind, crossover trial." *Journal of Neurology, Neurosurgery & Psychiatry* 1999; 66(2):251-2.
- Dalocchio C. et al. "Gabapentin vs. amitriptyline in painful diabetic neuropathy: an open-label pilot study." *Journal of Pain & Symptom Management* 2000;20(4):280-5.
- Serpell M.G. "Gabapentin in neuropathic pain syndromes: a randomised, double-blind, placebo-controlled trial." *Pain* 2002;99(3):557-66.
- Rosenstock J. et al. "Pregabalin for the treatment of painful diabetic peripheral neuropathy: A double-blind, placebo-controlled trial." *Pain* 2004;110(3):628-638.
- Dworkin R.H. et al. "Pregabalin for the treatment of postherpetic neuralgia: A randomized, placebo-controlled trial." *Neurology* 2003;60(8):1274-1283.
- Lesser H. et al. "Pregabalin relieves symptoms of painful diabetic neuropathy: A randomized controlled trial." *Neurology* 2004;63(11):2104-2110.
- Backonja M. et al. "Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial." *JAMA* 1998;280(21):1831-6.
- Thienel U. et al. "Topiramate in painful diabetic polyneuropathy: Findings from three double-blind placebo-controlled trials." *Acta Neurologica Scandinavica* 2004;110(4):221-231.
- Caraceni A. et al. "Gabapentin for neuropathic cancer pain: a randomized controlled trial from the Gabapentin Cancer Pain Study Group." *J Clin Oncol* 2004;22(14): 2909-17.
- Raskin P. et al. "Topiramate vs placebo in painful diabetic neuropathy: Analgesic and metabolic effects." *Neurology* 2004;63(5):865-873.
- Rowbotham M. et al. "Gabapentin for the treatment of postherpetic neuralgia: a randomized controlled trial." *JAMA* 1998;280(21):1837-42.
- Rice A.S. et al. "Gabapentin in postherpetic neuralgia: a randomised, double blind, placebo controlled study." *Pain* 2001;94(2):215-24.
- Simpson D.M. et al. "Lamotrigine for HIV-associated painful sensory neuropathies: a placebo-controlled trial." *Neurology* 2003;60(9):1508-14.
- Backonja M. et al. "Gabapentin dosing for neuropathic pain: evidence from randomized, placebo-controlled clinical trials." *Clinical Therapeutics* 2003;25(1):81-104.
- Vestergaard P. et al. "Fracture risk associated with use of antiepileptic drugs." *Epilepsia* 2004;45(11):1330-7.
- Ibanez L. et al. "Population-based drug-induced agranulocytosis." *Arch Intern Med* 2005;165(8):869-74.
- Lin M.S. et al. "Risk estimates for drugs suspected of being associated with Stevens-Johnson syndrome and toxic epidermal necrolysis: a case-control study." *Intern Med J* 2005;35(3):188-90.
- Goodwin F.K. et al. "Suicide risk in bipolar disorder during treatment with lithium and divalproex." *JAMA* 2003;290(11):1467-73.
- Rzany B. et al. "Risk of Stevens-Johnson syndrome and toxic epidermal necrolysis during first weeks of antiepileptic therapy: a case-control study. Study Group of the International Case Control Study on Severe Cutaneous Adverse Reactions." *Lancet* 1999;353(9171):2190-4.
- Tohen M. et al. "Blood dyscrasias with carbamazepine and valproate: a pharmacoepidemiological study of 2,228 patients at risk." *Am J Psychiatry* 1995;152(3):413-8.
- Poolsup N. et al. "Systematic overview of lithium treatment in acute mania." *J Clin Pharm Ther* 2000;25(2):139-56.
- Bridle C. et al. "A rapid and systematic review and economic evaluation of the clinical and cost-effectiveness of newer drugs for treatment of mania associated with bipolar affective disorder." *Health Technology Assessment* 2004;8(19):iii-109.
- Macritchie K.A. et al. "Valproic acid, valproate and divalproex in the maintenance treatment of bipolar disorder (Cochrane Review)." *The Cochrane Library*, Issue 1. Chichester, UK: John Wiley & Sons, Ltd. 2004.
- Tondo L. et al. "Rapid-cycling bipolar disorder: effects of long-term treatments." *Acta Psychiatr Scand* 2003;108(1):4-14.
- Bahk W.M. et al. "Topiramate and divalproex in combination with risperidone for acute mania: A randomized open-label study." *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 2005;29(1):115-121.
- Goswami U. et al. "Comparative efficacy and tolerability of lithium, carbamazepine and valproate in acute mania." *Journal of Psychopharmacology* 2001;15:A19; B4.
- Edwards K.R. et al. "Lamotrigine monotherapy improves depressive symptoms in epilepsy: a double-blind comparison with valproate." *Epilepsy & Behavior* 2001;2: 28-36.
- Alberti G.G. et al. "Efficacy and tolerability of gabapentin (GBP) and valproate (VPA) as an adjunct in the neuroleptic treatment of acute manic syndromes [abstract]." *Journal of the European College of Neuropsychopharmacology* 1999;9(Suppl 5):S210.
- Tohen M. et al. "Olanzapine versus divalproex in the treatment of acute mania." *American Journal of Psychiatry* 2002;159(6):1011-7.
- Greil W. et al. "The comparative prophylactic efficacy of lithium and carbamazepine in patients with bipolar I disorder." *International Clinical Psychopharmacology* 1999;14(5):277-81.
- Greil W. et al. "Lithium versus carbamazepine in the maintenance treatment of bipolar II disorder and bipolar disorder not otherwise specified." *International Clinical Psychopharmacology* 1999;14(5):283-5.
- Thies-Flechtner K. et al. "Effect of prophylactic treatment on suicide risk in patients with major affective disorders. Data from a randomized prospective trial." *Pharmacopsychiatry* 1996;29(3):103-7.
- Simhandl C. et al. "The comparative efficacy of carbamazepine low and high serum level and lithium carbonate in the prophylaxis of affective disorders." *Journal of Affective Disorders* 1993;28(4):221-31.
- Weisler R.H. et al. "A multicenter, randomized, double-blind, placebo-controlled trial of extended-release carbamazepine capsules as monotherapy for bipolar disorder patients with manic or mixed episodes." *J Clin Psychiatry* 2004;65(4):478-84.
- Weisler R.H. et al. "Extended-release carbamazepine capsules as monotherapy for acute mania in bipolar disorder: a multicenter, randomized, double-blind, placebo-controlled trial." *J Clin Psychiatry* 2005;66(3):323-30.
- Calabrese J.R. et al. "A double-blind placebo-controlled study of lamotrigine monotherapy in outpatients with bipolar I depression. Lamictal 602 Study Group." *Journal of Clinical Psychiatry* 1999;60(2):79-88.
- Mellegers M.A. et al. "Gabapentin for neuropathic pain: systematic review of controlled and uncontrolled literature." *Clin J Pain* 2001;17(4):284-95.
- Wiffen P. et al. "Anticonvulsant drugs for acute and chronic pain (Cochrane Review)." *The Cochrane Library* 2004;(Issue 1).
- Rockliff B.W. et al. "Controlled sequential trials of carbamazepine in trigeminal neuralgia." *Archives of Neurology* 1966;15:129-36.
- Gilron I. et al. "Topiramate in trigeminal neuralgia: a randomized, placebo-controlled multiple crossover pilot study." *Clin Neuropharmacol* 2001;24(2):109-12.
- McCleane G.J. "Intravenous infusion of phenytoin relieves neuropathic pain: a randomized, double-blinded, placebo-controlled, crossover study." *Anesth Analg* 1999;89(4):985-8.
- Bone M. et al. "Gabapentin in postamputation phantom limb pain: a randomized, double-blind, placebo-controlled, cross-over study." *Regional Anesthesia & Pain Medicine* 2002;27(5):481-6.
- McCleane G.J. "Does gabapentin have an analgesic effect on background, movement and referred pain? A randomised, double-blind, placebo controlled study." *Pain Clinic* 2001;13:103-107.
- McCleane G.J. "Gabapentin reduces chronic benign nociceptive pain: A double-blind, placebo-controlled cross-over study." *Pain Clinic* 2000;12:81-85.
- Andrews D.G. et al. "The comparative cognitive side-effects of lithium, carbamazepine and combined lithium-carbamazepine in patients treated for affective disorders." *Hum. Psychopharmacol.* 1990;5:41-45.
- Lima M.S. et al. "Antidepressants for cocaine dependence. "Antidepressants for cocaine dependence (Cochrane Review)." *The Cochrane Library*, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.
- Brown D. et al. "Carbamazepine compared to haloperidol in acute mania." *Int Clin Psychopharmacol* 1989;4(3):229-38.
- Parsons B. et al. "Gabapentin: A pooled analysis of adverse events from three clinical trials in patients with postherpetic neuralgia." *American Journal Geriatric Pharmacotherapy* 2004;2(3):157-162.
- Sabatowski R. et al. "Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia: Results of a randomised, placebo-controlled clinical trial." *Pain* 2004;109(1-2):26-35.
- Qiu Y. et al. "Once-a-day controlled-release dosage form of divalproex sodium I: formulation design and in vitro/in vivo investigations." *J Pharm Sci* 2003;92(6):1166-73.

Balance, investigators, collaborators, Geddes JR, et al. Lithium plus valproate combination therapy versus monotherapy for relapse prevention in bipolar I disorder (BALANCE): a randomized open-label trial. *Lancet* 2010 Jan 30;375(9712):385-95.

Bowden C, Gogus A, Grunze H, Haggstrom L, et al. A 12-week, open, randomized trial comparing sodium valproate to lithium in patients with bipolar I disorder suffering from a manic episode. *Int Clin Psychopharmacol* 2008 Sep;23(5):254-62.

Bowden CL, Mosolov S, Hranov L, Chen E, et al. Efficacy of valproate versus lithium in mania or mixed mania: a randomized, open 12-week trial. *Int Clin Psychopharmacol* 2010 Mar;25(2):60-7.

El-Mallakh RS, Salem MR, Chopra A, Mickus GJ, et al. A blinded, randomized comparison of immediate-release and extended-release carbamazepine capsules in manic and depressed bipolar subjects. *Ann Clin Psychiatry* 2010 Feb;22(1):3-8.

El-Mallakh RS, Salem MR, Chopra AS, Mickus GJ, et al. Adverse event load in bipolar participants receiving either carbamazepine immediate-release or extended-release capsules: a blinded, randomized study. *Int Clin Psychopharmacol* 2009 May;24(3):145-9.

Hirschfeld RMA, Bowden CL, Vigna NV, Wozniak P, et al. A randomized, placebo-controlled, multicenter study of divalproex sodium extended-release in the acute treatment of mania. *J Clin Psychiatry* 2010 Apr;71(4):426-32.

Juruena MF, Ottoni GL, Machado-Vieira R, Carneiro RM, et al. Bipolar I and II disorder residual symptoms: oxcarbazepine and carbamazepine as add-on treatment to lithium in a double-blind, randomized trial. *Prog Neuropsychopharmacol Biol Psychiatry* 2009 Feb 1;33(1):94-9.

Kakkar AK, Rehan HS, Unni KES, Gupta NK, et al. Comparative efficacy and safety of oxcarbazepine versus divalproex sodium in the treatment of acute mania: a pilot study. *Eur Psychiatry* 2009 Apr;24(3):178-82.

Kemp DE, Gao K, Ganocy SJ, Elhaj O, et al. A 6-month, double-blind, maintenance trial of lithium monotherapy versus the combination of lithium and divalproex for rapid-cycling bipolar disorder and Co-occurring substance abuse or dependence. *J Clin Psychiatry* 2009 Jan;70(1):113-21.

Kruger S, Sarkar R, Pietsch R, Hasenclever D, et al. Levetiracetam as monotherapy or add-on to valproate in the treatment of acute mania—a randomized open-label study. *Psychopharmacology (Berl)* 2008 Jun;198(2):297-9.

McElroy SL, Martens BE, Creech RS, Welge JA, et al. Randomized, double-blind, placebo-controlled study of divalproex extended release loading monotherapy in ambulatory bipolar spectrum disorder patients with moderate-to-severe hypomania or mild mania. *J Clin Psychiatry* 2010 May;71(5):557-65.

Shafti SS, Shahveisi B. Comparison between lithium and valproate in the treatment of acute mania. *J Clin Psychopharmacol* 2008 Dec;28(6):718-20.

Van der Loos MLM, Mulder PGH, Hartong EGTM, Blom MBJ, et al. Efficacy and safety of lamotrigine as add-on treatment to lithium in bipolar depression: a multicenter, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2009 Feb;70(2):223-31.

Vieta E, Cruz N, Garcia-Campayo J, de Arce R, et al. A double-blind, randomized, placebo-controlled prophylaxis trial of oxcarbazepine as adjunctive treatment to lithium in the long-term treatment of bipolar I and II disorder. *Int J Neuropsychopharmacol* 2008 Jun;11(4):445-52.

Smith B, Peterson K, Fu R, Thakurta S, et al. Drugs for Fibromyalgia. Drug Effectiveness Review Project 2011:<http://derp.ohsu.edu/about/final-document-display.cfm>.

Selph S, Carson S, Fu R, Thakurta S, et al. Drugs for Neuropathic Pain. Drug Effectiveness Review Project 2011:<http://derp.ohsu.edu/about/final-document-display.cfm>.