

Consumer Reports BEST BUY DRUGS®

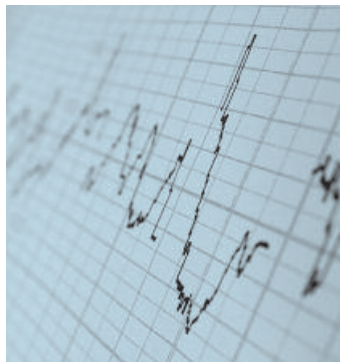
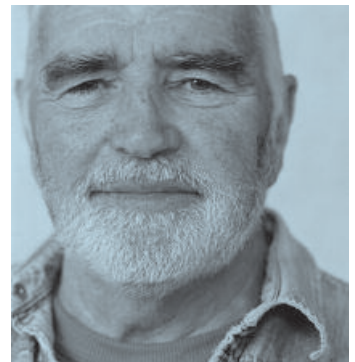
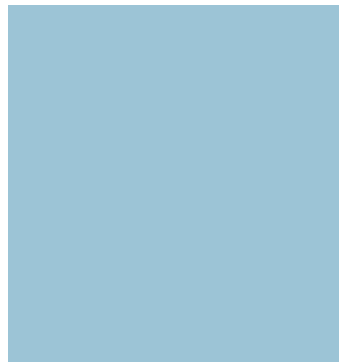
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Treating Bipolar Disorder, Nerve Pain,
and Fibromyalgia:

The Anticonvulsants

Comparing Effectiveness, Safety, and Price



Our Recommendations

Anticonvulsant drugs are prescribed widely to treat a range of medical conditions. Among those are bipolar disorder, fibromyalgia, and nerve pain (neuralgia) caused by injuries or diseases that adversely affect the nervous system.

Overall, the evidence supporting the use of anticonvulsants by people with one (or more) of the three conditions is mixed. Other treatment options exist for all three which may work better than an anticonvulsant. Some anticonvulsants have been linked to clear clinical benefits, however, and several have been approved by the Food and Drug Administration (FDA) for use by people with bipolar disorder, nerve pain, or, in the case of one drug, fibromyalgia.

The anticonvulsants are generally safe, but in rare cases can cause serious side effects. Newer anticonvulsants marketed since the late 1990s have sometimes been put forth as safer and posing less risk of adverse effects than older ones. Studies do not support this conclusion.

Taking cost, dosing convenience, and the evidence for effectiveness, safety, and adverse effects into consideration, we have chosen the following as *Consumer Reports Best Buy Drugs* if your doctor and you have decided to try an anticonvulsant:

- *Generic carbamazepine* – for treating the mania phase of bipolar disorder or trigeminal neuralgia, a type of nerve pain that affects facial nerves
- *Generic valproic acid* – for treating the mania phase of bipolar disorder
- *Lamotrigine (Lamictal)* – for treating both the mania and depressive phases of bipolar disorder
- *Generic gabapentin* – for treating the nerve pain associated with diabetes or herpes zoster infection (shingles)
- *Pregabalin (Lyrica)* – for treating the nerve pain associated with diabetes or herpes zoster infection (shingles)

Lamictal, Lyrica and higher doses of both generic gabapentin and generic valproic acid are relatively costly medicines. But the evidence for their effectiveness, for the indications given, justify their selection as *Best Buys* providing value for the money.

This report was released and last updated in September 2007.

Welcome

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

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

Some anticonvulsants have been around for decades. The first one – phenytoin (Dilantin) – was approved in the U.S. in 1946. Phenytoin was followed by carbamazepine (Carbatrol, Tegretol), ethotoin (Peganone), 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.

In the 1990s, a new group of “second-generation” anticonvulsants was developed. Some doctors had prescribed the older drugs for non-seizure-related conditions, but the development of the new drugs spurred a greatly increased use of both the old and the new anticonvulsants to treat conditions other than seizures. This primarily involved people with bipolar disorder or pain that had its’ origins in nervous system damage, trauma, or dysfunction – so called nerve pain.

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

Fibromyalgia is a syndrome involving symptoms such 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 and – since there is no definitive diagnostic test for it – has been a controversial, somewhat uncertain diagnosis for some years. (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(s)	Available as a Generic?
Carbamazepine	Tegretol	Yes
	Carbatrol, Epitol, Equetro, Tegretol-XL	No
Ethotoin	Peganone	No
Phenytoin, Phenytoin sodium	Dilantin, Phenytek	Yes
Divalproex, Valproic acid	Depakene, Depakote, Depakote ER	Yes*

*Valproic acid (Depakene) is available as a generic.

The Newer Anticonvulsants		
Generic Name	Brand Name(s)	Available as a Generic?
Gabapentin	Neurontin	Yes
Lamotrigine	Lamictal, Lamictal CD	Yes*
Levetiracetam	Keppra	No
Oxcarbazepine**	Trileptal	No
Pregabalin	Lyrica	No
Tiagabine	Gabitril	No
Topiramate	Topamax	No
Zonisamide	Zonegran	Yes

* Only the dissolving tablet was available as a generic at the time this report was prepared.

**A chemical variation of carbamazepine

Some of the anticonvulsants have been approved by the Food and Drug Administration (FDA) to treat bipolar disorder, some kinds of nerve pain, and fibromyalgia. Namely, 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 been approved to treat fibromyalgia.

But many of the other anticonvulsants are also widely prescribed “off-label” (without FDA approval) to treat these conditions. While many drugs are prescribed effectively off-label, we advise using extra caution with such prescriptions. Indeed, some of the anticonvulsants (old and new) have been for years on lists of drugs that are being too widely prescribed off-label without scientific support. Some have also been abused and misused by young people who obtain them “on the street.”

Importantly, anticonvulsants are only one of many treatment options for bipolar disorder, nerve pain, or fibromyalgia. For example, the most commonly prescribed drugs for bipolar disorder are lithium and antipsychotics. And non-drug treatment for bipolar disorder includes hospitalization and professional counseling.

Nerve pain and fibromyalgia are also commonly treated with other drug and non-drug measures. These include antidepressants, opioid pain relievers, non-opioid pain relievers (acetaminophen and the NSAID drugs), a pain-relieving drug called tramadol (Ultram), skin patches that contain pain killers, transcutaneous electrical nerve stimulation (TENS), acupuncture, physical therapy, occupational therapy, biofeedback, exercise, relaxation therapy, meditation, and hypnosis.

It is very common for people with bipolar disorder, nerve pain or fibromyalgia to try several different medicines and/or combinations of medicines and non-drug treatments before finding adequate relief.

This report is based on a comprehensive analysis of the medical evidence. More than 1,600 studies were identified and screened. From these, the analysis focused on 110 studies that directly compared one anticonvulsant drug to another or to other commonly-used medicines or a placebo.

This report is part of a Consumers Union and *Consumer Reports* project to help you find safe, effective medicines 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 www.CRBestBuyDrugs.org.

This report was released and last updated in September 2007.



What Are the Anticonvulsants and Who Needs Them?

No one knows exactly how the anticonvulsants work to ease neuropathic (nerve) pain or help people with bipolar disorder or fibromyalgia. They are widely thought to work by affecting chemicals in the brain and nervous system called neurotransmitters, and by reducing or blocking electrical signals in nerve and brain cells.

The anticonvulsants do not all work in the same way. Indeed, each drug operates in a different way and affects individuals differently. People may respond poorly to one anticonvulsant but quite well to another, for example.

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

The evidence is 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, and very subjective symptoms – ones that can only be gauged by the patient's reported experience. Bipolar disorder, nerve pain, and fibromyalgia are all conditions which, in large part, involve the patient's own judgment of the relief they get from a drug.

If you are diagnosed with one of these three conditions, your need for an anticonvulsant may not be all that clear-cut. Unlike high blood pressure, diabetes, or cholesterol-lowering drugs, for example – where the vast majority of people who take a drug will experience a clinical benefit that can be measured objectively by simple tests – some people taking an anticonvulsant may get significant benefit from it while others get little or no benefit.

Also, as discussed above, other drugs and treatments exist for all three conditions. In some cases, those should be the initial or primary therapy. That may be

What is Bipolar Disorder?

Everyone has times when they feel "up" and times when they feel "down." For some people, though, swings in mood can be extreme, last much longer than normal, and occur for no apparent (life circumstance) reason. Such people – about six million in the U.S. – are said to have bipolar disorder, also called manic depression.

Bipolar disorder has two distinct phases: mania and depression. In most cases, either mood lasts for several weeks and there is often an in-between period with a "normal" or stable mood. About a third to half of 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 have shorter periods of mania (from a week to several weeks) and longer periods of depression (from several weeks to months).

Common symptoms of mania episode:

- Feelings of extreme happiness and well-being
- Increased talkativeness
- Racing thoughts and ideas
- Reduced need for sleep
- Irritability
- Increase in risky behaviors
- Increased impulsiveness

Common symptoms of depressive episode:

- Feelings of unhappiness and despair
- Loss of interest/pleasure in previously-enjoyed activities
- Decreased energy, extreme fatigue
- Trouble sleeping: going to sleep, staying asleep, and/or early morning awakening
- Difficulty concentrating
- Irritability/restlessness
- Increases or decreases in appetite
- Suicidal thoughts/attempts

the case for most people with bipolar disorder, for example, for whom lithium may be a better choice than an anticonvulsant.

The need for anticonvulsants in treating nerve pain is more widely accepted – and complex. Three anticonvulsants – carbamazepine, gabapentin, and pregabalin – have been approved for treating nerve pain. But, as with bipolar disorder, other drug and non-drug treatments are available that could be better for selected patients and eliminate the need for an anticonvulsant. In addition, the long-term effectiveness

and safety of anticonvulsants in treating nerve pain have not been well studied.

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. Thus, such drugs have a long track record for this use, but they also pose a fairly high risk of side effects. We further discuss Lyrica's use to treat fibromyalgia in the next section.

What is Nerve Pain?

More than 100 types of nerve pain exist. It can occur in patients with diabetes, human immunodeficiency virus (HIV), herpes zoster infection (shingles), cancer, amputation of a limb, alcoholism, or tissue inflammation. Nerve pain can also occur following stroke, multiple sclerosis (MS), spinal cord injury, surgery, or trauma to the body.

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

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

- *Diabetic neuropathy* – a common complication of diabetes. About half of the 16 to 20 million people with diabetes in the U.S. will suffer from neuropathy, and the incidence increases over time. About 20 percent of 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 nerve in the area is called the trigeminal nerve.
- *Postherpetic neuralgia* – is caused by nerve inflammation that occurs during and after an attack of shingles, which in turn is caused by the same virus that causes chickenpox (herpes zoster). As many as one million people in the U.S. at any one time suffer from this form of nerve pain.
- *Cancer-associated neuralgia* – can be a direct result of the cancer impinging on nerves or a cancer in a part of the nervous system itself. But it can also occur as a result of the treatment of cancer with certain kinds of chemotherapy, which can damage nerve cells.
- *Compression neuropathy* – occurs when a nerve is pressed by a slipped disc (sciatica) or by a ligament (carpal tunnel syndrome).
- *Phantom limb neuropathy* – is a unique type of pain experienced by people who have had a limb amputated; they continue to feel sensations and pain emanating from the limb that is no longer there.

What is Fibromyalgia?

Fibromyalgia is a term encompassing a constellation of symptoms that includes 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 be diagnosed with depression, anxiety, rheumatoid arthritis, lupus, Lyme disease, and chronic fatigue syndrome.

The cause is unknown, although it has been linked (inconclusively) to viral infection, exposures to toxins, and physical or emotional trauma.

An estimated three to six million people in the U.S. have been diagnosed with fibromyalgia; some 80 percent are women. It is still a controversial diagnosis, with suspicions that some people diagnosed with fibromyalgia actually have something else or do not meet the diagnostic criteria for fibromyalgia. Many insurers are skeptical of the diagnosis and only reluctantly reimburse for expenses incurred in treating it.

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

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

People with fibromyalgia symptoms often see many doctors. If you suspect you may have fibromyalgia, the important thing is to see a doctor who is familiar with the condition and can conduct a thorough examination to either confirm the diagnosis or rule it out, and help you.



Choosing an Anticonvulsant – Our *Best Buy* Picks

If you and your doctor have arrived at a decision to try an anticonvulsant, this section will help you decide which one might be best clinically, and give you the most value for your health care dollar. Each of the three conditions is discussed in turn below.

One overriding issue with the anticonvulsant drugs is whether the newer ones are better than the older ones. There is no consistent, clear evidence for this. Indeed, there are no good studies at all that directly compare the effectiveness and safety of the older anticonvulsants to the newer ones for treating bipolar disorder, nerve pain, or fibromyalgia.

The older drugs have the advantage of having been prescribed for many years, and many doctors know their strengths, weaknesses, and risks quite well – and perhaps better than the newer drugs.

However, the older drugs do not work for everyone and can have serious side effects. In addition, the older drugs can require frequent dosing to be effective – needing to be taken three to four times a day and in fairly high doses involving many pills.

The newer drugs have their own set of problems and side effects, but also distinctive clinical strengths. In general, they require less frequent dosing, but you still may 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, although three are now available as generics which will likely become less expensive over time. (See Table 3 on page 14.)

In choosing our *Best Buys*, we take into account the evidence for effectiveness, side effects, safety, and costs. In addition, we consider dosing convenience. With these medicines in particular, your doctor may think dosing convenience is very important – and choose a more expensive medicine on that basis. You may want to have a conversation with your doctor if the cost of a medicine is a more important factor for you than your doctor may appreciate – for example, if you are uninsured or your co-pay for one anticonvulsant is higher than another.

Note also that the dosing regimens for the 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 very important to communicate with your doctor about whether you feel the drug is helping or not. With pain relief, that's easy to know. If it is 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 have reached a full dose, if there is no response, discuss discontinuing the drug with your doctor and trying another.

Bipolar disorder

The evidence for effectiveness in treating bipolar disorder is strongest for carbamazepine, valproic acid (and divalproex), and lamotrigine. Carbamazepine and valproic acid have proven benefits in stabilizing mood during bipolar manic episodes, while lamotrigine has been used successfully in managing bipolar patients in both the manic and depressive phases.

Up to about 70 percent of patients taking carbamazepine and 60 percent taking valproic acid/divalproex can expect to experience a noticeable decrease in manic symptoms after about three weeks of treatment. In some cases, carbamazepine may yield noticeable improvements after only seven days or so.

Lamotrigine (Lamictal) is the only anticonvulsant proven effective for treating depressive episodes of bipolar disorder, and also as a “maintenance therapy” to stabilize mood when taken for three weeks or longer. Over half of people got some benefit after taking the drug for seven weeks, with a reduction in both manic and depressive symptoms. But effectiveness fell off somewhat over the longer-term, with about a third (36%) of people in one study staying “in remission” (with stabilized mood) a year and a half after treatment started.

The treatment of so-called “rapid-cycling” bipolar disorder with anticonvulsants has been less studied. In

one study, lamotrigine showed positive modest benefits after six months of treatment, with measurable mood stabilization for up to 40 percent of people.

Notably, the American Psychiatric Association (APA) includes valproic acid and lamotrigine in their most recent guidelines for first-line treatment of bipolar disorder.

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

- *Generic carbamazepine* – for treating the mania phase of bipolar disorder
- *Generic valproic acid* – for treating the mania phase of bipolar disorder
- *Lamotrigine (Lamictal)* – for treating both the mania and depressive phases of bipolar mania

Nerve pain

The effectiveness of the anticonvulsants in treating nerve pain has been well studied only for selected drugs – most notably, carbamazepine, gabapentin (Neurontin), and pregabalin (Lyrica). Studies have focused on postherpetic neuralgia, diabetic neuropathy, and trigeminal neuralgia. (See page 7.)

Consistent evidence supports the effectiveness of gabapentin and pregabalin in treating postherpetic neuralgia. The evidence gives pregabalin a slight edge, with 28 percent to 58 percent of people with the condition experiencing obvious pain relief. Gabapentin brought relief to between 32 percent and 43 percent of patients in studies.

In addition, studies found that both drugs improve sleep patterns and overall quality of life in people who have postherpetic neuralgia. Only one older anticonvulsant – valproic acid/divalproex – has shown promise as an effective treatment for postherpetic neuralgia. But the studies so far are inconclusive.

For the treatment of diabetic neuropathy, the quantity and quality of evidence is strongest for pregabalin (Lyrica). This medicine is also the only anticonvulsant

approved by the FDA for the treatment of diabetic neuropathy. But gabapentin has also been found effective and is a less expensive medicine available now as a generic. Both drugs, studies have found, can yield pain relief within the first two weeks of treatment – a critical criteria for people who experience the most intense episodes of nerve pain.

No large scale studies have evaluated any of the older anticonvulsants in treating diabetic neuropathy. That could be because these drugs are generics and their makers do not have the money to support extensive clinical trials.

In contrast, an older anticonvulsant, carbamazepine, is the only anticonvulsant that has been proven effective in relieving the pain of trigeminal neuralgia. (Oxcarbazepine has also been shown effective, and was better tolerated by patients in some studies. But it is substantially more expensive than carbamazepine.) Carbamazepine is FDA-approved for this use and is widely considered as a first-line treatment. 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 to get relief, which raises the risk of side effects.

Two other anticonvulsants have shown promise in studies in treating other types of nerve pain: lamotrigine for nerve pain associated with strokes, diabetic neuropathy, and HIV-related neuropathy; and topiramate (Topamax) for diabetic neuropathy.

Gabapentin has shown promise in treating spinal cord injury pain, HIV-related neuropathy, and nerve pain associated with cancer. This drug has been widely prescribed “off-label” for these conditions, but – unfortunately – the evidence is still not conclusive on how much it helps.

The longer-term effectiveness of the 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 measurement of pain relief using numerical rating scales. In addition, very few studies have evaluated whether the anticonvulsants improve overall quality of life. And no studies have directly compared the older and newer drugs.

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

- *Generic gabapentin* – for treating postherpetic and diabetic neuropathy
- *Pregabalin (Lyrica)* – for treating postherpetic and diabetic neuropathy
- *Generic carbamazepine* – for treating trigeminal neuralgia

Fibromyalgia

The review of the evidence on which this report is based identified no studies that evaluated the use of the anticonvulsants in treating fibromyalgia. However, that review was conducted prior to the approval by the FDA in June 2007 of the drug pregabalin (Lyrica) to treat fibromyalgia.

That approval was based primarily on a study of 1,800 people. In the study, 78 percent of people who took the drug reported “any improvement” in pain relief versus 48 percent who took a placebo. Treatment was over 14 weeks. In follow-up over an additional three months, more people (53%) continued to take Lyrica and report pain relief than placebo (33%).

Lyrica is an important addition to the drug treatment options for fibromyalgia. However, you and your doctor should continue to weigh the pros and cons of all the treatment options for this condition. For many people diagnosed with this condition, drugs other than Lyrica may be a better initial choice. That said, many doctors may now choose to try Lyrica first, or sooner rather than later if you are not getting help from another drug.

Lacking any strong evidence comparing the various drugs to treat fibromyalgia, we do not choose any *Best Buy* anticonvulsants for this condition.

Table 1. Effectiveness of Selected Anticonvulsants*

Drug	Bipolar Disorder	Nerve Pain
Carbamazepine	Good mood stabilization in mania episodes in up to 70% of people in studies.	Very good results against trigeminal neuralgia (intense facial pain); 75% get some relief and about one in three get almost complete pain relief.
Valproic Acid	Clear improvement and moderate stabilization during mania episodes in up to 60% of people in studies.	Pain relief in up to 60% of people with postherpetic pain in studies.
Gabapentin	No evidence	<ul style="list-style-type: none"> - Strong results in treating postherpetic neuralgia – with one out of every four patients having moderate overall improvement compared to 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.

Table 1. Effectiveness of Selected Anticonvulsants* (continued)

Drug	Bipolar Disorder	Nerve Pain
Pregabalin (Lyrica)	No evidence	<ul style="list-style-type: none"> - Pain relief in 28% to 58% of people with postherpetic neuralgia. - Pain relief in 40% to 48% of patients with diabetic neuropathy.
Lamotrigine (Lamictal)	Remission from depressed episodes lasting at least 7 months in one key study. Other studies have found relief from rapid cycling and mania episodes lasting 2 months longer than with other drugs.	<ul style="list-style-type: none"> - Possible effectiveness for nerve pain that follows a stroke. - Possible effectiveness against pain associated with trigeminal neuralgia.
Topiramate (Topamax)	No evidence	<ul style="list-style-type: none"> - Some evidence for effectiveness in treating diabetic neuropathy, with 36% of patients experiencing obvious pain relief.

* Results presented are based on a range of studies.

Side Effects and Safety Issues with the Anticonvulsants

All the anticonvulsant drugs can cause side effects. Some can be severe, but the vast majority are not. Between 44 percent and 95 percent of people taking an anticonvulsant experience at least one side effect. The most common are dizziness, sleepiness, and nausea. For some of the newer anticonvulsants, swelling of hands and feet, weight gain, blurry vision, trouble concentrating and memory lapses are also common side effects.

Most people who start taking an anticonvulsant continue on the medicine. However, the “discontinuation” rates of the medicines do differ and are presented in Table 2 on page 13. Discontinuation rates are considered a good barometer of how well a medicine is tolerated over time.

Some anticonvulsants have been linked to serious adverse effects. While rare, the risk of severe problems should always be weighed against the benefits of treatment. See table 2 below for mention of some severe problems that can develop with these medicines.

The anticonvulsants are often taken alongside other drugs, and two anticonvulsants are sometimes taken together. This demands extra vigilance on your part and that of your doctor. Always be sure to tell your doctor about all the other medicines you are taking.

The newer anticonvulsants have sometimes been put forth as safer and having fewer side than the older ones. No good studies have tested this directly and studies that have compared the drugs do not support such a general conclusion. The types of side effects and safety issues do differ between the older and newer drugs, but drugs within each group also pose different risks. Your doctor must assess your individual circumstances.

Table 2. Side Effects and Safety Profile of Selected Anticonvulsants

Drug	Withdrawal Due to Adverse Events*	Comments
Carbamazepine	9-13%	<ul style="list-style-type: none"> - 30% can expect to experience some dizziness, a higher percentage than with some of the newer anticonvulsants, such as gabapentin and lamotrigine. - Requires monitoring level of the drug in the blood. - Less suitable for people with histories of bone marrow deficiencies or liver disease. - Rare risk of drop in blood cell and platelet counts, rash, and liver failure.
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 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 doctor. - Some studies have found a higher risk of suicide death in bipolar patients taking these drugs compared to lithium. - Linked to rare cases of certain birth defects - Periodic monitoring of blood level of the drug recommended.
Gabapentin	5-19%	<ul style="list-style-type: none"> - Risk of weight gain and edema
Lamotrigine (Lamictal)	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 also higher with larger doses, and a too-rapid increase in dose. - Any rash while taking should prompt immediate contact with your doctor. - Rare hypersensitivity can leading to multi-organ failure or serious blood diseases. - Should not be taken by pregnant women or women who may become pregnant due to elevated risk of fetal malformations. - Periodic monitoring of blood level of the drug recommended.
Pregabalin (Lyrica)	11%-32%	<ul style="list-style-type: none"> - Use cautiously in patients with pre-existing heart conditions. Possible weight gain and edema may lead to increased risk of heart failure in this population. - Only on market since 2004, long-term effects unknown.
Topiramate (Topamax)	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 when taking. - Linked to more clinically important weight loss (19%-38% of patients) than any weight changes associated with other anticonvulsants. - Can lead to decreased effectiveness of oral contraceptives. - Interacts with multiple other drugs.

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

Table 3. The Anticonvulsants – Dosing and Costs

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
	<i>Carbamazepine 200mg tablet</i>	Epitol	Two-Five	400-1,000mg	\$14-\$35
	<i>Carbamazepine 200mg tablet</i>	Tegretol	Two-Five	400-1,000mg	\$58-\$145
CR BEST BUY	<i>Carbamazepine 200mg tablet</i>	Generic	Two-Five	400-1,000mg	\$6-\$15
	<i>Carbamazepine 100mg chewable tablet</i>	Tegretol	Two-Six	200-600mg	\$36-\$108
CR BEST BUY	<i>Carbamazepine 100mg chewable tablet</i>	Generic	Two-Six	200-600mg	\$16-\$48
	<i>Carbamazepine 100mg SR tablet⁵</i>	Carbatrol	Two-Four	200-400mg	\$98-\$196
	<i>Carbamazepine 200mg SR tablet</i>	Carbatrol	Two-Four	400-800mg	\$90-\$180
	<i>Carbamazepine 300mg SR tablet</i>	Carbatrol	Two-Three	600-900mg	\$92-\$138
	<i>Carbamazepine 100mg SR tablet</i>	Tegretol XR	Two-Four	200-400mg	\$36-\$72
	<i>Carbamazepine 200mg SR tablet</i>	Tegretol XR	Two-Four	400-800mg	\$64-\$128
	<i>Carbamazepine 400mg SR tablet</i>	Tegretol XR	Two-Four	400-1,600mg	\$120-\$240
	<i>Carbamazepine 100mg SR tablet</i>	Equetro	Two-Four	200-400mg	\$100-\$200
	<i>Carbamazepine 200mg SR tablet</i>	Equetro	Two-Four	400-800mg	\$106-\$212
	<i>Carbamazepine 300mg SR tablet</i>	Equetro	Two-Four	600-1,200mg	\$96-\$192
	<i>Divalproex 125mg tablet</i>	Depakote	Two-Four	250-500mg	\$66-\$132
	<i>Divalproex 125mg</i>	Depakote Sprinkle	Two-Four	250-500mg	\$62-\$124
	<i>Divalproex 250mg tablet</i>	Depakote	Two-Four	500-1,000mg	\$114-\$228
	<i>Divalproex 500mg tablet</i>	Depakote	Two-Four	1,000-2,000mg	\$202-\$404
	<i>Divalproex 250mg SR tablet</i>	Depakote ER	One-Four	250-1,000mg	\$57-\$228
	<i>Divalproex 500mg SR tablet</i>	Depakote ER	One-Four	500-2,000mg	\$94-\$376
	<i>Ethotoin 250mg tablet</i>	Peganone	Five-Ten	1,250-2,500mg	\$220-\$440
	Gabapentin 100mg capsule	Neurontin	Two-Four	200-400mg	\$48-\$96
	Gabapentin 300mg capsule	Neurontin	Two-Four	600-1,200mg	\$120-\$240
	Gabapentin 400mg capsule	Neurontin	Two-Four	800-1,600mg	\$140-\$280
	Gabapentin 600mg tablet	Neurontin	One-Three	600-1,800mg	\$109-\$327
	Gabapentin 800mg tablet	Neurontin	One-Two	800-1,600mg	\$133-\$266
CR BEST BUY	Gabapentin 100mg tablet	Generic	Two-Four	200-400mg	\$38-\$76
CR BEST BUY	Gabapentin 300mg tablet	Generic	Two-Four	600-1,200mg	\$88-\$176
CR BEST BUY	Gabapentin 400mg tablet	Generic	Two-Four	800-1,600mg	\$92-\$184
CR BEST BUY	Gabapentin 600mg tablet	Generic	Two-Four	1,200-2,400mg	\$122-\$244
CR BEST BUY	Gabapentin 800mg tablet	Generic	Two-Three	1,600-2400mg	\$140-\$210
CR BEST BUY	Gabapentin 100mg capsule	Generic	Two-Four	200-400mg	\$32-\$64
CR BEST BUY	Gabapentin 300mg capsule	Generic	Two-Four	600-1,200mg	\$88-\$176
CR BEST BUY	Gabapentin 400mg capsule	Generic	Two-Four	800-1,600mg	\$80-\$160

Table 3. The Anticonvulsants – Dosing and Costs

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	Lamotrigine 25mg tablet	Lamictal	One-Two	25-50mg	\$166-\$332
CR BEST BUY	Lamotrigine 100mg tablet	Lamictal	One-Two	100-200mg	\$170-\$340
CR BEST BUY	Lamotrigine 150mg tablet	Lamictal	One-Two	150-300mg	\$188-\$376
CR BEST BUY	Lamotrigine 200mg tablet	Lamictal	One-Two	200-400mg	\$\$198-\$396
CR BEST BUY	Lamotrigine 5mg dissolving tablet	Lamictal	One-Three	5-15mg	\$162-\$486
CR BEST BUY	Lamotrigine 5mg dissolving tablet	Generic	One-Three	5-15mg	\$123-\$369
CR BEST BUY	Lamotrigine 25mg dissolving tablet	Generic	One-Two	25-50mg	\$128-\$256
	Levetiracetam 250mg tablet	Keppra	Three-Six	750-1,500mg	\$285-\$570
	Levetiracetam 500mg tablet	Keppra	Two-Six	1,000-3,000mg	\$220-\$660
	Levetiracetam 750mg tablet	Keppra	Two-Four	1,500-3,000mg	\$308-\$616
	Levetiracetam 1,000mg tablet	Keppra	One-Three	1,000-3,000mg	\$212-\$636
	Oxcarbazepine 150mg tablet	Trileptal	Three-Five	450-750mg	\$189-\$315
	Oxcarbazepine 300mg tablet	Trileptal	Two-Five	600-1,500mg	\$222-\$555
	Oxcarbazepine 600mg tablet	Trileptal	Two-Four	1,200-2,400mg	\$394-\$788
CR BEST BUY	Pregabalin 25mg capsule	Lyrica	Two-Three	50-75mg	\$168-\$252
CR BEST BUY	Pregabalin 50mg capsule	Lyrica	Two-Three	100-150mg	\$162-\$243
CR BEST BUY	Pregabalin 75mg capsule	Lyrica	Two-Three	150-225mg	\$164-\$246
CR BEST BUY	Pregabalin 100mg capsule	Lyrica	Two-Three	200-300mg	\$162-\$243
CR BEST BUY	Pregabalin 150mg capsule	Lyrica	Two-Three	300-450mg	\$160-\$240
CR BEST BUY	Pregabalin 200mg capsule	Lyrica	Two	400mg	\$154
CR BEST BUY	Pregabalin 225mg capsule	Lyrica	Two	450mg	\$154
CR BEST BUY	Pregabalin 300mg capsule	Lyrica	Two	600mg	\$160
	<i>Phenytoin 50mg tablet</i>	Dilantin	Three-Four	150-200mg	\$45-\$60
	<i>Phenytoin 50mg chewable tablet</i>	Dilantin	Three-Four	150-200mg	\$51-\$68
	<i>Phenytoin 30mg ER capsule⁶</i>	Dilantin	One-Four	30-120mg	\$14-\$56
	<i>Phenytoin 100mg ER capsule</i>	Dilantin	One-Four	100-400mg	\$13-\$39
	<i>Phenytoin 100mg tablet</i>	Generic	Three-Four	300-400mg	\$36-\$48
	<i>Phenytoin 100mg ER capsule</i>	Generic	One-Four	100-400mg	\$10-\$40
	<i>Phenytoin 200mg ER capsule</i>	Dilantin	One-Three	200-600mg	\$27-\$81
	<i>Phenytoin 300mg ER capsule</i>	Phenytek	One-Three	300-900mg	\$39-\$117
	Tiagabine 2mg tablet	Gabitril	Two-Four	4-8mg	\$232-\$464
	Tiagabine 4mg tablet	Gabitril	Two-Four	8-16mg	\$232-\$464
	Tiagabine 12mg tablet	Gabitril	Two-Four	24-48mg	\$272-\$544

Table 3. The Anticonvulsants – Dosing and Costs

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
Tiagabine 16mg tablet	Gabitril	Two-Three	32-48mg	\$346-\$519
Topiramate 25mg tablet	Topamax	Two	50mg	\$164
Topiramate 50mg tablet	Topamax	Two	100mg	\$316
Topiramate 100mg tablet	Topamax	Two	200mg	\$426
Topiramate 200mg tablet	Topamax	Two	400mg	\$494
Topiramate 15mg capsule	Topamax	Two	30mg	\$176
Topiramate 25mg capsule	Topamax	Two	50mg	\$220
<i>Valproic Acid 250mg capsule</i>	Depakene	Two-Eight	500-2,000mg	\$184-\$736
CR BEST BUY <i>Valproic Acid 250mg tablet</i>	Generic	Two-Eight	500-2,000mg	\$24-\$96
CR BEST BUY <i>Valproic Acid 250mg capsule</i>	Generic	Two-Eight	500-2,000mg	\$15-\$120
Zonisamide 25mg capsule	Zonegran	Two-Four	50-100mg	\$56-\$112
Zonisamide 50mg capsule	Zonegran	Two-Four	100-200mg	\$96-192
Zonisamide 100 mg capsule	Zonegran	Two-Four	200-400mg	\$214-\$428
Zonisamide 25mg capsule	Generic	Two-Four	50-100mg	\$40-\$80
Zonisamide 50mg capsule	Generic	Two-Four	100-200mg	\$68-\$136
Zonisamide 100mg capsule	Generic	Two-Four	200-400mg	\$122-\$244

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 may be less than or greater than the range indicated in this table. With many drugs in this tablet, it is also common to start at a lower dose for two weeks or more and have the dose increased over the next few weeks. Many of the drugs are ineffective or only marginally effective at too low a dose.
3. See note 2.
4. Prices reflect nationwide retail averages for April 2007. They are rounded to the nearest dollar. Information derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Health, Pharmaceutical Audit Suite.
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 your doctor and you arrive at a decision about which anticonvulsant drug or dose is best for you.

Bear in mind that many people are reluctant to discuss the cost of medicines with their doctors and that studies show doctors do not routinely take price into account when prescribing medicines. Unless you bring it up, your doctors may assume that cost is not a factor for you.

Many people (including many physicians) also believe that newer drugs are always or almost always better. While that's a natural assumption to make, the fact is that it's not true. Studies consistently show that many older medicines are as good as, and in some cases better than, newer medicines. Think of them 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 prescription drugs are indeed more effective and safer. Talk with your doctor about the pluses and minuses of newer versus older medicines, including generic drugs.

Prescription medicines go "generic" when a company's patents on a drug 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 today about half of all prescriptions in the U.S. 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 may not always tell each other which drugs have been prescribed for you.

Second, it is very common for doctors today to prescribe several medicines for you before finding one that works well or best, mostly because people vary in their response to prescription drugs.

Third, more and more people today take several prescription medications, nonprescription drugs and supplements all at the same time. Many of these interact in ways that can be very dangerous.

And fourth, the names of prescription drugs—both generic and brand—are often hard to pronounce and remember.

For all these reasons, it's important to keep a list of the drugs you are taking, both prescription and nonprescription and including dietary supplements.

Always be sure, too, that you understand the dose of the medicine being prescribed for you and how many pills you are expected to take each day. Your doctor should tell you this information. When you fill a prescription at the pharmacy, or if you get it by mail, you may want to check to see that the dose and the number of pills per day on the pill bottle match the amounts that your doctor told you.

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 the anticonvulsant medicines. 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 15-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP's analysis of the anticonvulsants forms the basis for this report. A consultant to *Consumers Reports 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 the 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 site were obtained from a healthcare information company that tracks

the sales of prescription drugs in the U.S. Prices for a drug can vary quite widely, even within a single 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 2007.

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 the other anticonvulsants
- Have a safety record equal to or better than other anticonvulsants
- Be priced reasonably relative to other anticonvulsants or deliver value for the money if a relatively costly medicine

The *Consumers Reports Best Buy Drugs* methodology is described in more detail in the methods section at www.CRBestBuyDrugs.org.

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 to create a fair marketplace. Its website is www.consumersunion.org. The magazine's website is www.consumerreports.org.

Consumer Reports Best Buy Drugs™ is a public education project administered by Consumers Union. Two outside sources of generous funding made the project possible. They are a major grant from the Engelberg Foundation, a private philanthropy, and a supporting grant from the National Library of Medicine, part of the National Institutes of Health. A more detailed explanation of the project is available at www.CRBestBuyDrugs.org.

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We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Best Buy Drugs* website is accurate and describes generally accepted clinical practices. If we find, or are alerted to, an error, we will correct this as quickly as possible. However, *Consumer Reports* and its authors, editors, publishers, licensors and any suppliers cannot be responsible for errors or omissions, or any consequences from the use of the information on this site.

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