

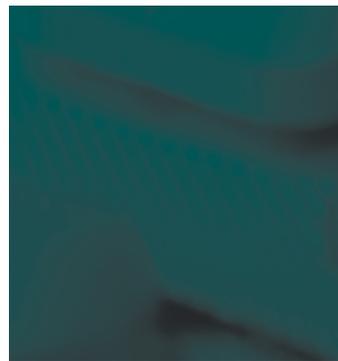
BEST BUY DRUGS



Evaluating Prescription Drugs Used to
Treat Muscle Spasms and Spasticity:

The Muscle Relaxants

Comparing Effectiveness, Safety, and Price



Our Recommendations – A Summary

The skeletal muscle relaxants are a diverse set of drugs that are used for treating muscle spasticity or spasms, which can cause pain and interfere with your functional ability. Spasticity, or having stiff, rigid muscles with exaggerated reflexes, generally lasts a long time. It arises from conditions affecting the brain and/or spinal cord, such as cerebral palsy, multiple sclerosis, and stroke. Muscle spasms, on the other hand, are usually temporary and are associated with conditions affecting the muscles, bones, and associated structures, such as tension headaches, back or neck pain, and fibromyalgia.

While these are widely prescribed drugs, the evidence supporting the effectiveness of the nine available muscle relaxants is sparse, and some studies are of questionable quality. Many of the available studies are old and do not meet current standards. While the available evidence indicates that the drugs can help relieve symptoms, the poor quality of the research makes it difficult to draw firm conclusions about whether any one drug is superior to the others. Also, most of these medicines cause sedation as a side effect, and some of them pose a risk of serious problems, such as liver toxicity and addiction.

Muscle spasticity

Taking into consideration all of the evidence on muscle relaxants for spasticity, our *Best Buy* pick is:

- Generic baclofen tablet

Baclofen costs between \$27 and \$60 for a 30-day supply, so you could save a significant amount of money over some of the more expensive brand-name muscle relaxants, which can cost \$200 to up to \$486 a month. If you are unable to tolerate baclofen, we recommend trying generic tizanidine.

Muscle spasms

If you have a musculoskeletal problem—such as headache, back or neck pain—fibromyalgia or other conditions that cause spasms that have not responded to nondrug therapies, then pain relievers such as acetaminophen (Tylenol and generics) or non-steroidal anti-inflammatory drugs, or NSAIDS (aspirin, ibuprofen,

naproxen) are a reasonable first option. The muscle relaxants have not been found to be any better than these painkillers for providing relief. Plus, the muscle relaxants can cause sedation and other serious side effects. If you can't tolerate acetaminophen or NSAIDs because of kidney or liver problems, bleeding ulcers or heart issues, then you may want to consider trying a muscle relaxant.

If you and your doctor have decided to try a muscle relaxant to treat muscle spasms, taking all of the evidence into consideration, we chose the following as a *Best Buy*:

- Generic cyclobenzaprine tablet

Cyclobenzaprine is supported by the strongest body of evidence. Also, it is available in a generic form that costs \$8 to \$15 for a seven-day course, which makes it one of the least expensive muscle relaxants and significantly less expensive than brand-name ones that can run more than \$100. If cyclobenzaprine is not effective or causes you side effects that you can't tolerate, you could try methocarbamol or chlorzoxazone, both of which are available as inexpensive generics. We recommend avoiding carisoprodol (Soma) because it is associated with a high risk of abuse and addiction potential not seen with other skeletal muscle relaxants.

In addition to sedation, the most common side effects associated with muscle relaxants include weakness or fatigue, dizziness, and dry mouth.

This report was released in December 2009.

Welcome

This report compares the effectiveness, safety, and cost of a class of medications known as skeletal muscle relaxants. The term skeletal refers to the fact that there are three types of muscles in the body: skeletal, smooth, and cardiac. This group of drugs generally works only on the skeletal muscles, which power the movements of the skeleton. This is a diverse set of drugs that don't share a chemical structure or have the same mechanism of action. They are grouped together because they have been approved by the U.S. Food and Drug Administration (FDA) for treating similar conditions and disorders.

The result is that each medication may affect you—in terms of benefits and side effects—quite differently. In fact, many people are unaware that muscle relaxants are approved by the FDA to treat one of two very different types of underlying conditions: muscle spasticity due to conditions affecting the brain and/or spinal cord, such as cerebral palsy, multiple sclerosis, and stroke; and muscle spasms from conditions affecting the muscles, bones and associated structures, such as tension headaches, back or neck pain, or fibromyalgia. Spasticity is often a chronic condition that may last for years. Conversely, muscle spasms generally don't last very long, or may occur only on occasion.

Although some of the muscle relaxants are used to treat both conditions, nearly all of the muscle relaxants have only been well-studied for one condition or the other.

Another issue that complicates the evaluation of muscle relaxants is that many of the available studies are old and don't meet current standards for quality research. And because many of the muscle relaxants are older drugs that are available as generic medicines, there is little incentive for drug manufacturers to sponsor new studies. The result is that despite the widespread use of muscle relaxant drugs, the evidence among several drugs is sparse or inadequate for consumers or their doctors to compare benefits and harms.

There are nine muscle relaxants available in tablets or capsules. As you can see in Table 1, on page 5, all but a few are available in generic forms. A few are available in combination with aspirin, codeine, and/or caffeine.

Muscle relaxants are just one of the many types of medications that can be used to treat spasticity or spasms. Other medications that are sometimes used as muscle relaxants but don't carry FDA approval for this purpose include benzodiazepines, such as diazepam (Valium and generics), and botulinum toxin (Botox). Analgesics, such as acetaminophen and NSAIDs, are considered first line therapy for muscle spasms, and they may help relieve the pain associated with spasticity. Opioids,

Table 1. Muscle Relaxants

Generic Name	Form	Brand Name	Available as Generic?
Baclofen	Tablet	Lioresal	Yes
Carisoprodol	Tablet	Soma	Yes
Cyclobenzaprine HCl	Tablet	Fexmid,	No
	Tablet	Flexeril	Yes
	Continuous-release capsule	Amrix	No
Chlorzoxazone	Capsule	Parafon Forte DSC	Yes
Dantrolene	Capsule	Dantrium	Yes
Metaxalone	Tablet	Skelaxin	No
Methocarbamol	Tablet	Robaxin, Robaxin-750	Yes
Orphenadrine citrate	Tablet	Norflex	Yes
Tizanidine	Tablet and capsule	Zanaflex	Yes
Combination products			
Carisoprodol + aspirin	Tablet	Carisoprodol CPD	Yes
Carisoprodol + aspirin + codeine	Tablet	Carisoprodol CPD with codeine, Soma compound with codeine	Yes
Orphenadrine + aspirin + caffeine	Tablet	Norgesic Forte	Yes

such as codeine and morphine, are used as a last resort for treating these conditions because they can have dangerous side effects. Quinine has been used for treatment of muscle cramps, but you should be aware that the drug’s labeling warns against this use because the medicine can have serious and life-threatening side effects.

Some muscle relaxants can also be given intravenously or directly into the spine. However, this report focuses only on tablet or capsule (oral) muscle relaxants.

You may also want to talk with your doctor about other nondrug treatments for spasticity or muscle spasms. These include heating pads, exercise therapy, manipulation or mobilization, biofeedback or progressive relaxation, massage, yoga, and acupuncture.

What is the difference between muscle spasticity and muscle spasms?

Muscle spasticity is caused by damage to the brain or spinal cord. Normally, nerves in the brain and spinal cord help keep the muscles relaxed when you aren't using them. Conditions that affect the spinal cord or brain, such as cerebral palsy, multiple sclerosis, and stroke, can interfere with normal muscle relaxation, resulting in involuntary muscle spasms that can be very painful and impair your ability to walk, sleep, work, or just function normally. The muscles can also become excessively tense (hypertonia) and have overactive or overresponsive reflexes (hyperreflexia). This combination of symptoms is called the upper motor neuron syndrome. Severe cases can result in profound disability, including an inability to straighten out joints.

Among the muscle relaxants, only baclofen, dantrolene, and tizanidine are FDA approved for the treatment of spasticity. These three medications act by different mechanisms: Baclofen and tizanidine are thought to block certain nerve signals that "tell" muscles to contract, while dantrolene directly inhibits muscle contraction by decreasing the release of calcium, which is necessary to trigger muscle contraction.

Muscle spasms, on the other hand, occur in conditions which affect the muscles, bones, and associated tissues. These include headache, back or neck pain, and fibromyalgia or other conditions that cause chronic pain in the muscle tissues due to local factors involving the affected muscle groups, not damage to the nerves in the brain or spinal cord. With muscle spasms, unlike muscle spasticity, the muscles don't become excessively tense or show overactive reflexes. At the same time, fibromyalgia, headache, back or neck pain can be very painful and reduce your ability to function, and they are much more common conditions than having muscle spasticity.

What Are Muscle Relaxants and Who Needs Them?

Six of the muscle relaxants are FDA approved for treatment of muscle pain: carisoprodol, chlorzoxazone, cyclobenzaprine, metaxalone, methocarbamol, and orphenadrine. (Several trials have evaluated whether tizanidine is effective for treating musculoskeletal conditions, but it is only FDA approved for treatment of spasticity.) These drugs have very different pharmacological structures. Cyclobenzaprine is closely related to tricyclic antidepressants. Carisoprodol is broken down in the body into meprobamate, which is a drug classified as a controlled substance by the U.S. Drug Enforcement Agency due to its potential for addiction and abuse. Methocarbamol is structurally related to mephenesin, an older muscle relaxant that is no longer used because it was associated with blood clots and other dangerous side effects. Orphenadrine is derived from the antihistamine diphenhydramine (Benadryl), but generally causes more intensive side effects, such as dry mouth, sedation, urine retention, and increased eye pressure.

We don't know exactly how most of the muscle relaxants reduce muscle spasticity or spasms. Dantrolene, which blocks a key step involved in triggering muscle contraction, appears to have the most direct effect on the muscles. Other muscle relaxants appear to have more indirect effects. For example, baclofen blocks certain nerve signals to muscles, while tizanidine may cause effects that are similar to the high blood pressure drug clonidine. The sedative effect that most muscle relaxants cause may also be important. Many experts think that much of the benefit of these drugs may come from the sedation they induce in people.

When choosing among the many muscle relaxants, your doctor will consider whether you have muscle spasticity due to cerebral palsy, multiple sclerosis, stroke or other conditions that affect the brain and/or spinal cord; or muscle spasms tension headaches, back or neck pain, fibromyalgia or other conditions associated with chronic pain in muscle tissues.

Other factors your doctor will take into account include the severity of your symptoms, and the risk

of sedation, a concern for pilots, drivers, and people in other positions involving the use of heavy or dangerous equipment. Your doctor will also consider the side-effect profile of the different drugs—for example, the risk of liver toxicity or potential for addiction—and how you responded to muscle relaxants in the past if you previously took any. When you first start on one of these drugs, take the first dose at a time when you do not have to work or go anywhere, such as in the evening or on a weekend, to see how much sedation you experience. It is also a good idea to completely avoid alcohol while taking these medicines.

Muscle spasticity is generally considered a chronic condition, so muscle relaxants are often used on a scheduled, around-the-clock basis. But they also may be given as needed when the spasticity flares up. The dose that is used typically depends on whether the spasticity is continuous or is more episodic.

For treating muscle spasms due to conditions like back or neck pain, muscle relaxants are typically used on an as-needed, short-term basis. Although these medications are sometimes given long-term for treating these kinds of conditions, there is little evidence to show that chronic use actually improves symptoms.

Muscle Spasticity

Muscle spasticity caused by brain or spinal problems is difficult to measure. Standardized scales to assess it have been developed, but some experts think that they measure muscle tone more than spasticity. More importantly, measurements based on these kinds of scales may not correlate well with your symptoms or functional ability. The bottom line is that if you have an upper motor neuron syndrome, your need for a muscle relaxant should be based on how much pain and functional disability is caused by your spasticity, not solely on a spasticity score.

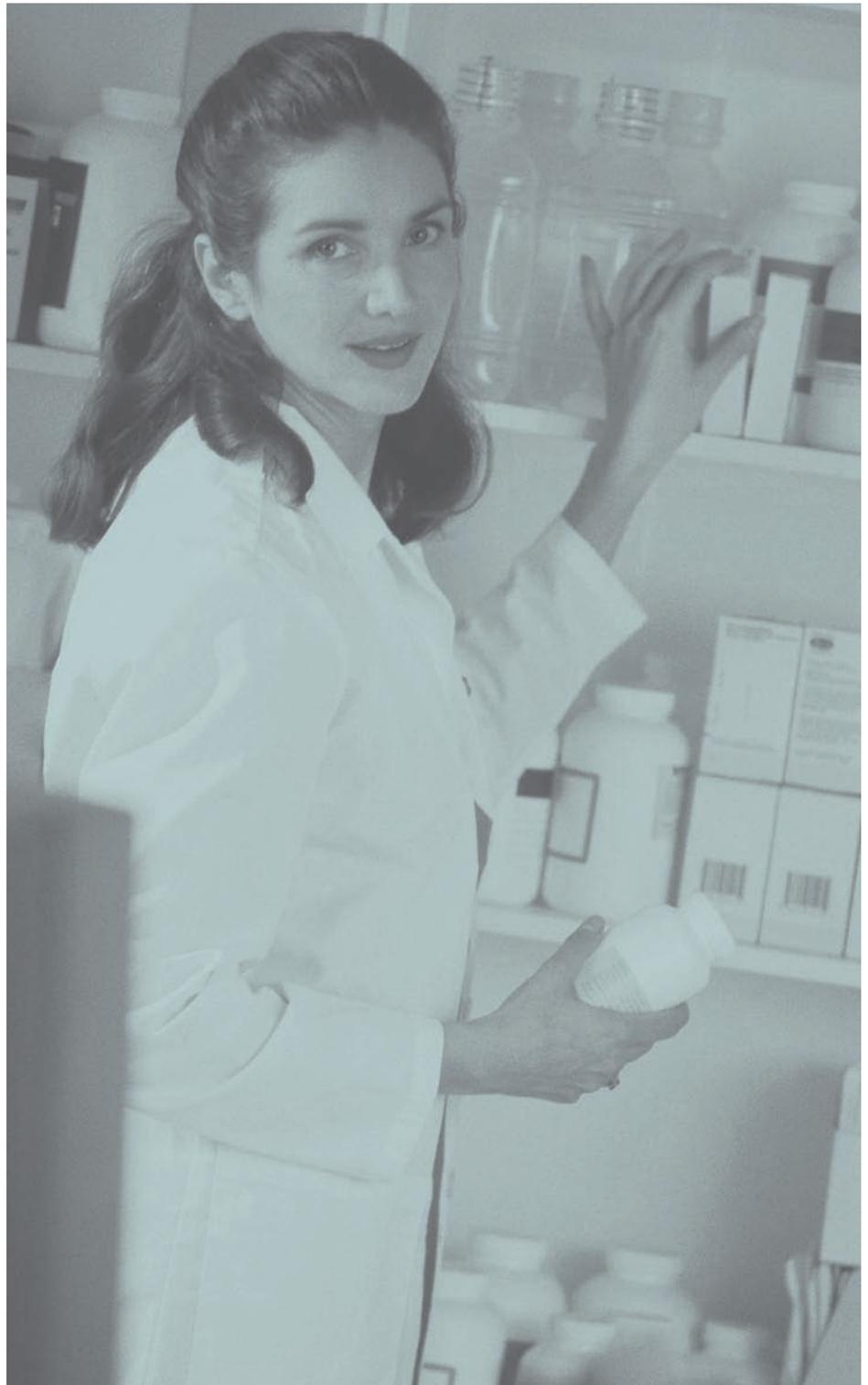
Muscle spasms

Many conditions that cause spasms, such as backache and headaches, are mild or self-limited, and

don't require specific therapy or drugs. In other cases, short courses of simple pain relievers, such as acetaminophen (Tylenol or generics) or NSAIDs, such as aspirin, ibuprofen (Advil and generics), or naproxen (Aleve and generics), are enough to bring relief. So you may want to try one of those nonprescription pain relievers first. Studies that compared simple pain relievers with muscle relaxants generally found little difference in how well they improved pain or function—but the muscle relaxants were associated with much more sedation.

In certain situations, however, muscle relaxants can be a preferred option. Some people may not be able to take acetaminophen if they have certain conditions, such as liver disease. And those with a history of bleeding ulcers or heart problems may not be able to take an NSAID. Others may find that their muscle-spasm symptoms make it difficult to sleep, so the sedation associated with the muscle relaxants is not necessarily an undesirable side effect. In some cases, muscle spasms may persist despite a trial of a simple pain reliever. In all these situations, a trial of a muscle relaxant may be appropriate. Most acute spasm episodes are limited to a few hours, days or weeks, and a short course of a muscle relaxant may be all you need to help you get through that period.

If the spasms last longer than a few weeks, you should discuss with your doctor whether you are truly benefiting from the muscle relaxant and whether it should be continued, or if alternative therapies should be tried.



Choosing a Muscle Relaxant – Our *Best Buy* Picks

Studies have found that muscle relaxants can relieve pain and improve symptoms associated with spasticity or spasms. (We discuss the evidence in detail beginning on page 12.) Some of the drugs in this class are better studied than others, so we favor those medicines because more is known about their effectiveness. All these drugs can cause side effects, including some dangerous ones, such as liver toxicity and addiction. But these issues have not been rigorously studied, so it's difficult to draw any conclusions about whether one muscle relaxant is superior to the others when it comes to safety. Tables 3 and 4 on pages 12 and 14 provide an overview of important considerations for each muscle relaxant.

Muscle Spasticity

Taking all the evidence on skeletal muscle relaxants into consideration, there are three medications that have been found to be effective for spasticity. Dantrolene is not a first-line drug because of its potential for serious liver injury. This leaves baclofen and tizanidine. Both of these medications are available in generic form, and as you can see from Table 5 beginning on page 15, a month's supply of baclofen costs \$27 to \$60, depending on the dose, and is less expensive than tizanidine, which costs \$72 to \$81. So, for patients with spasticity we recommend:

■ Generic baclofen tablet

Baclofen is FDA approved for treating spasticity due to multiple sclerosis and spinal cord injuries or diseases. Several studies support its effectiveness for treating spasticity associated with cerebral palsy, and there's no reason to think it wouldn't work for alleviating spasticity in general.

If you are unable to tolerate baclofen, we recommend trying tizanidine. Dantrolene should only be used as a last resort due to the serious liver risks associated with it.

Muscle spasms

If you have a musculoskeletal condition, such as headache, back or neck pain, fibromyalgia or other

conditions, that causes spasms that have not responded to nondrug therapies, then nonprescription pain relievers, such as acetaminophen (Tylenol or generics), or NSAIDs (aspirin, ibuprofen, naproxen) are a reasonable first option. As we've previously stated, the muscle relaxants have not been found to be any better than these for providing relief, and the relaxants can cause sedation and other serious side effects. But if you can't tolerate acetaminophen or NSAIDs because of liver problems, bleeding ulcers or heart issues, then you should discuss with your doctor whether trying a muscle relaxant would be appropriate for your situation.

If you and your doctor have decided to try a skeletal muscle relaxant for a musculoskeletal condition, based on all available evidence, we chose the following as a *Best Buy*:

■ Generic cyclobenzaprine tablet

Although several muscle relaxants appear to be effective for musculoskeletal conditions, our pick is based on the fact that cyclobenzaprine is supported by the strongest body of evidence. Also, it is available in a generic form that costs \$8 to \$15 for a seven-day course, which makes it one of the least expensive generic muscle relaxants and significantly less expensive than brand-name relaxants that can run more than \$100. (See Table 5 beginning on page 15 for cost comparison.) In addition, the 5 mg pill may be as effective as a 10 mg pill and have fewer side effects. Although a sustained-release formulation of cyclobenzaprine is available, it is much more expensive—at around \$91 for a seven-day supply—and hasn't been found to be more effective than the standard-release formulation. For most people, the substantial increase in cost isn't worth the greater convenience of once-a-day vs. three times daily dosing.

If cyclobenzaprine is not effective or causes side effects that you can't tolerate, you should switch to another muscle relaxant. Methocarbamol and chlorzoxazone are available as generics and cost less than \$15 for a 30-day supply. Keep in mind that the evidence for both of these drugs is fairly limited. Tizanidine, orphenadrine, and metaxalone are more

costly alternatives. Carisoprodol should be avoided if possible. Although it is available as a generic that costs about the same as methocarbamol and chlorzoxazone, it is associated with abuse and addiction potential not seen with other skeletal muscle relax-

ants. Your doctor would need to assess whether carisoprodol can be prescribed safely based on a number of factors, including whether you have a personal or family history of substance abuse or addiction, and what other medications you are taking.

Table 2. Muscle Relaxants: Key Points

Generic Name and Dose	Brand Name	Comments/Special Notes
For treatment of muscle spasticity		
Baclofen 5 mg, 10 mg or 20 mg three times daily	Lioresal	<ul style="list-style-type: none"> More weakness than tizanidine, but less dry mouth (similar sedation) Generic form available
Tizanidine 2 mg, 4 mg, or 6 mg (usually given three times daily, up to 24 mg/day)	Zanaflex	<ul style="list-style-type: none"> More dry mouth than baclofen, but less weakness (similar sedation) Occasional, usually nonserious liver enzyme abnormalities Generic form available
Dantrolene 25 mg, 50 mg, or 100 mg three-four times daily	Dantrium	<ul style="list-style-type: none"> Black-box warning for rare but potentially serious (occasionally fatal) liver toxicity Generic form available
For treatment of muscle spasms		
Cyclobenzaprine 5 mg or 10 mg three times daily	Flexeril	<ul style="list-style-type: none"> Effectiveness for musculoskeletal conditions supported by strongest body of evidence 5 mg as effective as 10 mg, with fewer side effects Generic form available
Cyclobenzaprine 15 mg or 30 mg once daily	Amrix	<ul style="list-style-type: none"> Sustained-release formulation resulting in once daily dosing Not found to be more effective than standard-release formulation No generic available
Carisoprodol 350 mg three times daily	Soma	<ul style="list-style-type: none"> Metabolized to meprobamate, a drug classified as a controlled substance because of abuse and addiction potential Case reports of abuse and addiction Use only with extreme caution
Chlorzoxazone 500 mg three times daily	Parafon Forte DSC	<ul style="list-style-type: none"> Rare cases of liver toxicity May cause red-orange urine but this is not harmful Generic form available
Metaxalone 400 mg and 800 mg three times daily	Skelaxin	<ul style="list-style-type: none"> Do not use in people with liver damage No generic form available
Methocarbamol 500 mg and 750 mg four times daily	Robaxin, Robaxin-750	<ul style="list-style-type: none"> May cause black, blue, or green urine, but this is not harmful Generic form available
Orphenadrine 100 mg	Norflex	<ul style="list-style-type: none"> Generic form available
Tizanidine 2 mg, 4 mg, or 6 mg (usually dosed three times daily, up to 24 mg/day)	Zanaflex	<ul style="list-style-type: none"> Approved for treatment of spasticity but also found to be effective for muscle spasm conditions Occasional, usually nonserious liver enzyme abnormalities Generic form available

The Evidence

This section presents more detailed information on the effectiveness and safety of muscle relaxants.

This report is based on an analysis of the scientific evidence on muscle relaxants. This systematic review was published in 2005, and a literature search was conducted to identify relevant new trials published since then. More than 120 studies were considered in the analysis, including 59 trials of muscle relaxants for treating spasticity, 52 for treating musculoskeletal conditions, nine systematic reviews and three meta-analyses.

How Effective Are Muscle Relaxants for Treating Spasticity?

For muscle spasticity due to upper motor neuron syndromes, the three FDA approved skeletal muscle relaxants—baclofen, dantrolene, and tizanidine—generally appear to be more effective than placebo for improving symptoms in short-term trials (less than 10 weeks in duration).

The other skeletal muscle relaxants, which are approved for treatment of other muscle conditions, have not been found to be more effective than placebo for treatment of spasticity.

Even for baclofen, dantrolene, and tizanidine, it is difficult to estimate your likelihood of improvement because many of the studies had methodological shortcomings; estimates were often imprecise due to small sample sizes (frequently 10 to 40 subjects); most of the studies used different (and often unproven) methods to measure spasticity and evaluate other outcomes; and there was some inconsistency between trials, with some finding no benefits. The few trials that evaluated effects on pain or function reported no clear differences between muscle relaxants vs. placebo, or inconclusive results. The largest placebo-controlled trial of baclofen found that 46 percent of the subjects experienced improvement in flexor spasms on baclofen compared with 16 percent on placebo after five weeks of treatment. A relatively large and well-conducted trial of tizanidine found that 28 percent of the patients who received this drug rated

Table 3. Muscle Relaxants: Overview of Evidence of Effectiveness*

Drug	Spasticity: Evidence showing benefit vs. placebo	Spasms: Evidence showing benefit vs. placebo
Baclofen	+++	Not shown to be beneficial
Dantrolene	+++	Not shown to be beneficial
Tizanidine	++	++
Carisoprodol	Not shown to be beneficial	+
Chlorzoxazone	Not shown to be beneficial	+
Cyclobenzaprine	Not shown to be beneficial	+++
Metaxalone	Not shown to be beneficial	+/-
Methocarbamol	Not shown to be beneficial	+
Orphenadrine	Not shown to be beneficial	+

* Key to chart: +++ = more than 10 randomized trials showing benefit; ++ = 5-9 randomized trials showing benefit; + = 2-4 randomized trials showing benefit; +/- = inconsistent evidence. "Not shown to be beneficial" means the drug is not FDA approved for this indication and there are only 0-2 trials showing benefit.

their overall outcome as “very good” or “good” after nine weeks compared with 14 percent of those who were given placebo.

In trials that directly compare tizanidine and baclofen, these drugs appear to be roughly equivalent for improving symptoms associated with spasticity.

There is insufficient evidence to adequately assess the comparative efficacy of dantrolene compared with tizanidine or baclofen. However, as in the section on side effects, dantrolene is not considered a first-line drug because of the risk of serious, and sometimes fatal, liver toxicity.

A number of trials have compared tizanidine, baclofen, and dantrolene with diazepam, a benzodiazepine that is often used (but not FDA approved) as a muscle relaxant. Diazepam should be reserved as a last resort because it can result in physical dependence, abuse, or addiction, and it is classified as a controlled substance by the U.S. Drug Enforcement Agency. In these trials, the three skeletal muscle relaxants appear to be similarly effective compared with diazepam.

There is insufficient evidence to determine if formulations that combine a skeletal muscle relaxant with another drug (such as aspirin, codeine, and/or caffeine) are any more effective than the skeletal muscle relaxant alone.

How Effective Are Muscle Relaxants for Treating Spasms?

The evidence on how well different muscle relaxants work to relieve pain from spasms caused by musculoskeletal conditions varies both in the quality and quantity of studies done. Cyclobenzaprine is the best studied of the skeletal muscle relaxants. In over 20 trials, cyclobenzaprine was consistently more effective than placebo on various measures of pain relief, functional ability, and muscle spasm.

Although cyclobenzaprine was studied for a number of musculoskeletal conditions, most trials involved patients with acute back or neck pain and lasted for a short-term period (less than four weeks). A meta-analysis of 10 trials of cyclobenzaprine vs. placebo to treat back or neck pain found that after 10 to 21 days, patients reported improving an average of about one point on 10-point pain or function scales. The longest trial found that cyclobenzaprine was no more effective than a placebo in patients with fibromyalgia at six months for likelihood of improvement. One trial found that cyclobenzaprine at a dose of 5 mg three times daily was as effective as cyclobenzaprine at 10 mg three times daily, but with less sedation. The benefits of a sustained-release formulation of cyclobenzaprine appear similar to the nonsustained release formulation, with the potential advantage of greater patient convenience due to less-frequent dosing.

Tizanidine is only FDA approved for the treatment of spasticity, but six studies have found it to also be

effective for spasms caused by musculoskeletal conditions.

Carisoprodol and orphenadrine have been studied less, with only four trials for each drug. The available evidence indicates that both drugs are more effective than placebo for spasms due to musculoskeletal conditions.

Chlorzoxazone and methocarbamol also appear to be effective for treating muscle spasms, but the evidence is limited to one trial for chlorzoxazone and three trials for methocarbamol.

The evidence on metaxalone is mixed. Some trials found no benefit compared with placebo, and others found some benefit. So we can't draw a conclusion about whether it is effective.

For dantrolene and baclofen, which are approved for treatment of spasticity, the evidence of benefits for spasms due to musculoskeletal conditions is very limited (one or two placebo-controlled trials).

There is insufficient evidence from head-to-head trials of different skeletal muscle relaxants for spasms to determine whether any one is superior to the others due to small numbers of trials for comparison and either no clear differences between drugs or methodological shortcomings in trials that found differences. A number of trials compared cyclobenzaprine to diazepam (a benzodiazepine) with no clear differences found.

There is also insufficient evidence to determine if formulations that combine a skeletal muscle relaxant with another drug (such as aspirin, codeine, and/or caffeine) are any more effective than the skeletal muscle relaxant alone.

Safety and Side Effects of Muscle Relaxants

In general, reliable evidence is lacking on the comparative safety of different skeletal muscle relaxants. In almost all trials, there was little or no evidence of rigorous adverse event assessment. One of the most common side effects of these drugs is sedation. Most patients experience some sedation with almost all skeletal muscle relaxants, though estimates vary substantially depending on how sedation is defined

and assessed. Table 4, below, lists the most common types of side effects reported in research studies that you should look for if you are taking a skeletal muscle relaxant.

Table 4. Most Common Side Effects of Muscle Relaxants

- Sedation or somnolence
- Weakness or fatigue
- Dizziness or lightheadedness
- Dry mouth

In head-to-head trials that compared tizanidine to baclofen for spasticity, both drugs were associated with roughly equivalent rates of sedation in anywhere from 20 percent to 80 percent of the patients, depending on the trial. Other side effects may be different, as most head-to-head trials of these two medications found tizanidine more likely to cause dry mouth and baclofen more likely to cause weakness. Nonetheless, there was no evidence that the overall rate of side effects (or side effects severe enough to result in stopping the drug) differs. Reversible elevations of liver tests have been reported with tizanidine, though this side effect usually doesn't cause any symptoms, and serious or fatal liver injury appears extremely rare. Other serious but rare side effects such as seizures, serious withdrawal, and overdose have been reported in case studies of baclofen.

Dantrolene is associated with a risk of serious (and occasionally fatal) liver toxicity. The drug carries a black-box warning—the FDA's strongest warning—on its label regarding this risk.

There is insufficient evidence to judge the comparative safety of other skeletal muscle relaxants in patients with spasticity.

As in the case of spasticity, reliable evidence is lacking on the comparative safety of different muscle relaxants for musculoskeletal conditions. In almost all trials, there was little or no evidence of rigorous adverse event assessment. Nonetheless, most patients will experience some sedation with almost

all skeletal muscle relaxants, though estimates vary substantially (typically 20 percent to 80 percent) depending on how sedation is defined and assessed.

There is insufficient evidence to judge whether any one skeletal muscle relaxant is safer than the others in patients with musculoskeletal conditions. Head-to-head data are limited and don't show any clear differences in risk of different side effects (or risk of intolerable side effects resulting in stopping the drug).

Although there is insufficient evidence to estimate the comparative risk of abuse or addiction, almost all reports of this complication have been in patients taking carisoprodol. This may be because carisoprodol is metabolized to meprobamate, a drug controlled by the Drug Enforcement Administration (DEA) because of its abuse and addiction potential. Carisoprodol is not controlled by the DEA, but some states control its use.

Other serious side effects appear rare and it is difficult to estimate their relative frequency. Tizanidine and chlorzoxazone have been associated with rare cases of serious liver damage when used for treating spasms.

One trial found that cyclobenzaprine 5 mg three times a day was just as effective as 10 mg three times a day, but was associated with fewer side effects, such as sedation.

Age, Gender, and Race Differences

There is not enough relevant evidence from the available studies to determine whether the muscle relaxants have different efficacy or safety profiles in younger or older people, different races, or men and women.

Table 5. – Cost Comparison of Muscle Relaxants

Generic Name and Dose	Brand Name	Typical dosing schedule ¹	Approved indication ¹	Average cost per 30 days of use (for spasticity) or per 7 days of use (for muscle spasms) ²
 Baclofen 10 mg tablet	Generic	Three times daily	Spasticity	\$27
 Baclofen 20 mg tablet	Generic	Three times daily	Spasticity	\$60
Carisoprodol 250 mg tablet	Soma	Three times daily	Spasms	\$84
Carisoprodol 350 mg tablet	Soma	Three times daily	Spasms	\$147
Carisoprodol 350 mg tablet	Generic	Three times daily	Spasms	\$11
Chlorzoxazone 500 mg tablet	Parafon Forte DSC	Three-four times daily	Spasms	\$63-\$84
Chlorzoxazone 500 mg tablet	Generic	Three-four times daily	Spasms	\$8-\$11
Cyclobenzaprine 5 mg tablet	Flexeril	Three times daily	Spasms	\$42
Cyclobenzaprine 10 mg tablet	Flexeril	Three times daily	Spasms	\$42
Cyclobenzaprine 7.5 mg	Fexmid	Three times daily	Spasms	\$105
 Cyclobenzaprine 5 mg	Generic	Three times daily	Spasms	\$15
 Cyclobenzaprine 10 mg	Generic	Three times daily	Spasms	\$8
Cyclobenzaprine 15 mg continuous delivery capsule	Amrix	Once daily	Spasms	\$91
Cyclobenzaprine 30 mg continuous delivery capsule	Amrix	Once daily	Spasms	\$91
Dantrolene 25 mg capsule	Dantrium	Three-four times daily	Spasticity	\$138-\$184
Dantrolene 50 mg capsule	Dantrium	Three-four times daily	Spasticity	\$165-\$220
Dantrolene 100 mg capsule	Dantrium	Three-four times daily	Spasticity	\$231-\$308
Dantrolene 25 mg capsule	Generic	Three-four times daily	Spasticity	\$111-\$148
Dantrolene 50 mg capsule	Generic	Three-four times daily	Spasticity	\$153-\$204
Dantrolene 100 mg capsule	Generic	Three-four times daily	Spasticity	\$198-\$264
Metaxalone 400 mg tablet	Skelaxin	Three times daily	Spasms	\$42
Metaxalone 800 mg tablet	Skelaxin	Three times daily	Spasms	\$105
Methocarbamol 500 mg tablet	Robaxin	Four times daily	Spasms	\$56
Methocarbamol 750 mg tablet	Robaxin-750	Four times daily	Spasms	\$56
Methocarbamol 500 mg tablet	Generic	Four times daily	Spasms	\$11
Methocarbamol 750 mg tablet	Generic	Four times daily	Spasms	\$14

Table 5. – Cost Comparison of Muscle Relaxants (continued)

Generic Name and Dose	Brand Name	Typical dosing schedule ¹	Approved indication ¹	Average cost per 30 days of use (for spasticity) or per 7 days of use (for muscle spasms) ²
Orphenadrine 100 mg tablet	Norflex	Twice daily	Spasms	\$42
Orphenadrine 100 mg tablet	Generic	Twice daily	Spasms	\$28
Tizanidine 2 mg tablet	Zanaflex	Three times daily	Spasticity	\$195
Tizanidine 4 mg tablet	Zanaflex	Three times daily	Spasticity	\$249
Tizanidine 2 mg capsule	Zanaflex	Three times daily	Spasticity	\$249
Tizanidine 4 mg capsule	Zanaflex	Three times daily	Spasticity	\$324
Tizanidine 6 mg capsule	Zanaflex	Three times daily	Spasticity	\$486
Tizanidine 2 mg tablet	Generic	Three times daily	Spasticity	\$81
Tizanidine 4 mg tablet	Generic	Three times daily	Spasticity	\$72
Carisoprodol/aspirin 200/325 mg tablet	Carisoprodol CPD	Three times daily	Spasms	\$42
Carisoprodol/aspirin/codeine 200/325/16 mg tablet	Carisoprodol CPD with codeine	Three times daily	Spasms	\$42
Methocarbamol/aspirin 400/325 mg tablet	Generic	Three times daily	Spasms	\$13
Orphenadrine/aspirin/caffeine 50/770/60 mg tablet	Norgesic forte	Three times daily	Spasms	\$63
Orphenadrine/aspirin/caffeine 25/385/30 mg tablet	Orphenadrine compound	Three times daily	Spasms	\$42
Orphenadrine/aspirin/caffeine 50/770/60 mg tablet	Orphenadrine compound	Three times daily	Spasms	\$63-\$84

1. As typically prescribed. The dose ranges and the drug's FDA approved indication are derived from drug-labeling information.

2. Prices reflect the nationwide retail average for August 2009, rounded to the nearest dollar. Information is derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Health, Pharmaceutical Audit Suite®. Wolters Kluwer Health is not involved in our analysis or recommendations.

Talking With Your Doctor

It's important for you to know that the information we present here 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 muscle-relaxant medication and dose is best for you, if one is warranted at all, and which gives 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 doctor, and that studies have found that 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 physicians) think that newer drugs are better. While that's a natural assumption to make, it's not true. Studies consistently find 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 vs. older medicines, including generic drugs.

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

Generics are 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 written 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, each may not be aware of medicines the others have prescribed.
- Second, since people differ in their response to medications, it is very common for doctors today to prescribe several medicines 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 drug or be 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 *written list* of all the drugs and supplements you are taking, and to periodically review this list with your doctors.

And always be sure 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* Drugs

Our evaluation is based in part on an independent scientific review of the studies and research literature on muscle-relaxant drugs conducted by a team of physicians and researchers at the Oregon Health & Science University Evidence-Based Practice Center. This analysis reviewed more than 120 studies, including 59 trials of muscle relaxants for treating spasticity, 52 for treating musculoskeletal conditions, nine systematic reviews and three meta-analyses. The analysis also included studies conducted by the drugs' manufacturers. This effort was conducted as part of the Drug Effectiveness Review Project, or DERP. DERP is a first-of-its-kind 11-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP's analysis of the muscle-relaxant drugs forms the basis for this report. An additional literature search was conducted to capture the most recent published studies available on muscle relaxants. A consultant to *Consumer 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 muscle-relaxant drugs is available at <http://www.ohsu.edu/ohsuedu/research/policycenter/DERP/about/final-products.cfm>. (This is a long and technical document written for physicians.)

The monthly costs we cite were obtained from a health-care information company that tracks the sales of prescription drugs in the U.S. Prices for a drug can vary quite widely. All the prices in this report are national averages based on sales in retail outlets. They reflect the cash price paid for a month's supply of each drug in August 2009.

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

- Be approved by the FDA to treat muscle spasticity or spasms.
- Be as effective as or more effective than other muscle relaxant medicines when prescribed appropriately according to FDA guidelines.
- Have a safety record equal to or better than other muscle relaxant medicines when prescribed appropriately.

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

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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 ConsumerReportsHealth.org/BestBuyDrugs.

We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Best Buy Drugs* Web site is accurate and describes generally accepted clinical practices. If we find, or are alerted to, an error, we will correct it as quickly as possible. But *Consumer Reports* and its authors, editors, publishers, licensers, and any 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 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.

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